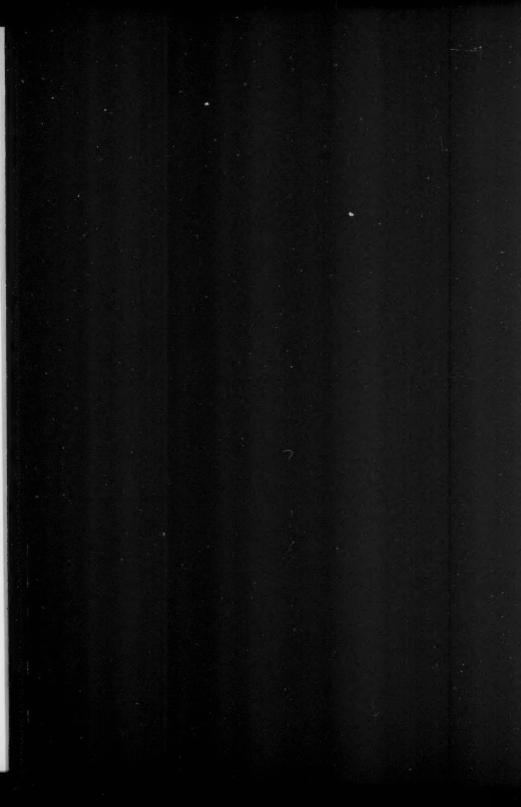
## **CONTENTS**

FRONTISPIECE—Allan H. Conney	х
INDUCTION OF DRUG-METABOLIZING ENZYMES: A PATH TO THE DISCOVERY OF MULTIPLE CYTOCHROMES P450, Allan H. Conney	1
PROTEIN FLEXIBILITY AND COMPUTER-AIDED DRUG DESIGN, Chung F. Wong and J. Andrew McCammon	31
RETINOID RECEPTORS AND THEIR COREGULATORS, Li-Na Wei	47
NOVEL PHARMACOLOGICAL APPROACHES TO MANAGE INTERSTITIAL LUNG FIBROSIS IN THE TWENTY-FIRST CENTURY, Shri N. Giri	73
NITRIC OXIDE-RELEASING DRUGS, Claudio Napoli and Louis J. Ignarro	97
2,5-HEXANDIONE-INDUCED TESTICULAR INJURY, Kim Boekelheide, Shawna L. Fleming, Theresa Allio, Michelle E. Embree-Ku, Susan J. Hall, Kamin J. Johnson, Eun Ji Kwon, Sutchin R. Patel, Reza J. Rasoulpour, Heidi A. Schoenfeld, and Stephanie Thompson	125
HUMAN EXTRAHEPATIC CYTOCHROMES P450: FUNCTION IN XENOBIOTIC METABOLISM AND TISSUE-SELECTIVE CHEMICAL TOXICITY IN THE RESPIRATORY AND GASTROINTESTINAL TRACTS, Xinxin Ding and Laurence S. Kaminsky	149
HORMESIS: THE DOSE-RESPONSE REVOLUTION, Edward J. Calabrese and Linda A. Baldwin	175
SIGNAL TRANSDUCTION—DIRECTED CANCER TREATMENTS, Edward A. Sausville, Yusri Elsayed, Manish Monga, and George Kim	199
REGULATORY MECHANISMS CONTROLLING GENE EXPRESSION MEDIATED BY THE ANTIOXIDANT RESPONSE ELEMENT,	
Truyen Nguyen, Philip J. Sherratt, and Cecil B. Pickett	233
MONOAMINE TRANSPORTERS: FROM GENES TO BEHAVIOR, Raul R. Gainetdinov and Marc G. Caron	261
GENETIC POLYMORPHISMS OF THE HUMAN MDR1 DRUG TRANSPORTER, Matthias Schwab, Michel Eichelbaum, and Martin F. Fromm	285
ACTIVATION OF THE ARYL HYDROCARBON RECEPTOR BY STRUCTURALLY DIVERSE EXOGENOUS AND ENDOGENOUS	
CHEMICALS, Michael S. Denison, and Scott R. Nagy	309

TRAFFICKING OF NMDA RECEPTORS, Robert J. Wenthold, Kate Prybylowski, Steve Standley, Nathalie Sans, and Ronald S. Petralia	335
TELOMERE INHIBITION AND TELOMERE DISRUPTION AS PROCESSES FOR DRUG TARGETING, Evonne M. Rezler, David J. Bearss, and Laurence H. Hurley	359
PHARMACOLOGY AND PHYSIOLOGY OF HUMAN ADRENERGIC RECEPTOR POLYMORPHISMS, Kersten M. Small, Dennis W. McGraw, and Stephen B. Liggett	381
GENE THERAPY WITH VIRAL VECTORS, Neeltje A. Kootstra and Inder M. Verma	413
K <sup>+</sup> CHANNEL STRUCTURE-ACTIVITY RELATIONSHIPS AND MECHANISMS OF DRUG-INDUCED QT PROLONGATION, Colleen E. Clancy, Junko Kurokawa, Michihiro Tateyama, Xander H.T. Wehrens, and Robert S. Kass	441
COMPLEMENTARY AND ALTERNATIVE THERAPEUTICS: RIGOROUS RESEARCH IS NEEDED TO SUPPORT CLAIMS, Jane F. Kinsel and Stephen E. Straus	463
CHALLENGING DOGMA: THRESHOLDS FOR GENOTOXIC CARCINOGENS? THE CASE OF VINYL ACETATE, J.G. Hengstler, M.S. Bogdanffy, H.M. Bolt, and F. Oesch	485
THE CAENORHABDITIS ELEGANS DOPAMINERGIC SYSTEM: OPPORTUNITIES FOR INSIGHTS INTO DOPAMINE TRANSPORT AND NEURODEGENERATION, Richard Nass and Randy D. Blakely	521
ALZHEIMER'S DISEASE: MOLECULAR UNDERSTANDING PREDICTS AMYLOID-BASED THERAPEUTICS, Dennis J. Selkoe and Dale Schenk	545
PROGRESS TOWARD CLINICAL APPLICATION OF THE NITRIC OXIDE—RELEASING DIAZENIUMDIOLATES, Larry K. Keefer	585
INNATE IMMUNE RESPONSES TO MICROBIAL POISONS: DISCOVERY AND FUNCTION OF THE TOLL-LIKE RECEPTORS, Bruce Beutler	609
THE ROLE OF DRUG TRANSPORTERS AT THE BLOOD-BRAIN BARRIER, A.G. de Boer, I.C.J. van der Sandt, and P.J. Gaillard	629
INDEXES	
Subject Index  Completing Index of Contributing Authors Volumes 30, 43	657 697
Cumulative Index of Contributing Authors, Volumes 39–43 Cumulative Index of Chapter Titles, Volumes 39–43	700

## **ERRATA**

An online log of corrections to Annual Review of Pharmacology and Toxicology chapters may be found at http://pharmtox.annualreviews.org/errata.shtml





## SUBJECT INDEX

A	and Alzheimer's disease,	superfamily, 285-86
ABC transporter(s), 285-86	551	and BL-induced lung
subfamily, 641	AcOM-PYRRO/NO, 588,	fibrosis, 76-77, 87
Ab4D5, 205-6	589	and cytoplasmic dyneins,
ACE-Inhibitors	and erectile dysfunction,	133
See Angiotensin converting	603	and OSI-774, 203
enzyme (ACE) inhibitors	Acrylonitrile	site antagonist(s), 204
Acetaldehyde	and carcinogenesis, 486	cancer treatments, 199,
exposure of tissues to,	Actinomycin D, 10	208
508-10	Action potential duration	Adenoviral (Ad) vector(s)
and exposure to vinyl	(APD), 443	Ad/AAV hybrid vectors,
acetate, 507-8, 512	and I <sub>Ks</sub> , 450-51, 454	427
Acetaminophen, 513-14	prolongation, 449, 452, 453	Ad/retrovirus hybrid
and cigarette smoking, 17	Activating signal	vectors, 427
and CYP genes, 156	cointegrator-2 (ASC2),	and adeno-associated viral
oxidative metabolism of,	58	(AAV) vectors, 414-15,
18, 19	Acute lymphoblastic	416
toxicity, 603	leukemia (ALL)	a death in clinical trials
Acetanilide, 6, 7	childhood, 298	with, 430
Acetic acid	Acute respiratory distress	development and
exposure of tissues to,	syndrome (ARDS), 601,	production, 424-26
508-10	602	and gene therapy, 414,
and exposure to vinyl	Adaptor-protein 2 (AP-2),	424-27
acetate, 507	634–35	properties of, 431
Acetone, 17	Adeno-associated viral	in the testis, 140
2-Acetoxybenzoate	(AAV) vectors	tropism and transduction,
2-(2-nitroxy)-butyl ester	development and	426-27
(NCX-4215), 103-4	production, 415-16	Adenovirus
2-Acetoxybenzoate 2-(2-	and gene viruses, 414-17	structure and replication,
nitroxy-methyl)-phenyl	and hemophilia B, 430	424
ester (NCX-4016),	properties of, 431	Adenylyl cyclase
103-4	structure and replication,	and adrenergic receptor
Acetyl salicylic acid, 465	414–15	polymorphisms (ARPs),
2-Acetylaminofluorene	tropism and transduction,	381, 384, 385, 386, 388,
(2-AAF), 498-99, 513	416–17	389-90, 399, 401, 403,
Acetylcholine, 107, 111	Adenosine deaminase (ADA)	404
and Alzheimer's disease,	deficiency	Adipose tissue
547	and gene therapy, 429-30	and $\beta_3$ adrenergic receptor
in C. elegans, 523	Adenosine triphosphate	(AR), 396, 397-98
Acetylcholinesterase	(ATP)	ADP-ribose
inhibitors	ATP-binding (ABC)	and BL-induced lung

61 76	and concentratement 100	position 27, 399
fibrosis, 76	and cancer treatment, 199,	position 27, 388
β-Adrenergic receptor	212–13	position 49, 382–83, 386
$(\beta$ -AR), 451–52	Allelopathy	position 64, 396
reduced responsiveness to,	and hormesis, 185	position 389, 383, 386
453	17-Allyl-amino-17-	position 399, 383
Adrenergic receptor (AR)	demethoxygeldanamycin	position 402, 383
antagonists	(17AAG), 199, 205	position 404, 383
and erectile dysfunction,	Alpha-tocopherol, 110, 111	position 418, 383
113	Alteration/deficiency in	position 492, 398
Adrenergic receptor	activation (Ada)	positions 301-3, 401
polymorphisms (ARPs),	transcription factor	Aminoazo dye(s)
381-404	coregulators, 56-57	and cigarette smoking, 17
$\alpha_1, 398-99$	Alternative medicine	and hydrocarbons, 3-5, 22
$\beta_1$ , 382–87	See Medicine(s),	4-Aminobiphenyl (4-ABP),
$\beta_2$ , 388–96	complementary and	499, 513
$\beta_3$ , 396–98	alternative	γ-Aminobutyric acid
$\alpha_{2A}$ , 399–400	Alzheimer's disease (AD),	(GABA)
α <sub>2B</sub> , 400–2	534, 545-76, 647	in C. elegans, 523
α <sub>2C</sub> , 402–4	amyloid hypothesis for,	Aminoguanidine, 84
Adrenomedullin (AM)	573-74	Aminopyrine, 5, 6
and P-glycoprotein, 640	and apolipoprotein (apo) E,	Amnestic symptoms
Adsorptive-mediated	633	and Alzheimer's disease,
transport (AMT), 631	and blood-brain barrier	546
Adverse	functionality, 632, 635	AMP-dependent protein
toxicological concept of,	clinical diagnosis of,	kinase (PKAs), 345, 347
175	546–47	AMPA receptor(s), 349
Aflacoxin B1	clinical syndrome, 546	GluR2/3, 350
formamidopyrimidine	current treatments, 551–52	and NMDA receptors
(AFB1-FAPY), 492	defining, 546–50	(NMDARs), 336, 342,
	familial, 549–50	344, 345, 347
Aflatoxin B1 (AFB1), 13,		
155, 485, 486, 491–94,	immunotherapy for,	and the synapse, 335–36
513	564–71, 573	AMPAkines, 270
activation of, 154	and melanotransferrin	Amphetamine(s)
hepatocarcinogen, 237, 238	(MTf), 645	and C. elegans, 525
AIDS	neurotransmitter	and dopamine transporter
and the blood-brain barrier,	phenotype, 547-48	(DAT)-KO mice, 270,
632	and oxidative stress, 253	271–72
Alanine, 39, 558	and potential	in mutant mice, 277
Albuterol, 392, 393, 394	neuroprotective strategies,	in norepinephrine
Alcohol ingestion, 22	552	transporter (NET)-KO
Alcoholics	and statins usage, 573	mice, 274
and drug tolerance, 19-20	Amino acid(s), 215	in serotonin transporter
Aldosterone	deletion, 400-4	(SERT)-KO mice, 273
renin-angiotensin-	and polymorphisms, 382,	Amyl nitrite, 99
	000	Amyloid $\beta$ -protein $(A\beta)$
aldosterone pathway,	383	Amylolu $\rho$ -protein $(A\rho)$
aldosterone pathway, 107	983 position 15, 385	Anyloid $\beta$ -protein $(A\beta)$ A $\beta$ 40

studies, 557, 560-61, in transgenic mouse 563-64, 571, 572 models, 550 immunization, 568 Amyloid hypothesis A842 for Alzheimer's disease, and Alzheimer's disease 573-74, 575-76 studies, 557, 560-61. AN-1792 562, 563-64, 571, 572 and Alzheimer's disease immunization, 564-68. studies, 570-71 570, 573 Aneurysm monoclonal antibodies brain, 598-99 directed against. ANGII, 106 568-69 ANGII type 1 (AT-1), 107  $A\beta$  plaques Angina monoclonal antibodies and aspirin, 465 directed against. and L-arginine, 110 569-70 Angina pectoris in Alzheimer's disease and chelation therapy, 471 brains, 546-47 treatment of, 99-100, 105-6 and amyloid  $\beta$ tprotein precursor (APP), 548-49 Angioplasty and cholesterol, 572-73 coronary, 100 restenosis after, 585, clearing it from the brain, 564-71 590-93 and familial Alzheimer's Angiotensin disease, 549, 550 renin-angiotensinimmunotherapy, 575 aldosterone pathway, neurotoxicity, 574 production of, 557, 565 Angiotensin II (ANGII), 100 and  $\beta$ -secretase, 555 Angiotensin converting and  $\gamma$ -secretase, 557, 558 enzyme (ACE) and  $\alpha$ -secretase, 571 inhibitors, 106-7 and y-secretase inhibitors, and nitrate tolerance, 101 561-64 Anion transporters, 641-42 Anterior deirids (ADEs) in transgenic mouse models, 550 and C. elegans, 523 Anthracycline, 206 Amyloid  $\beta$ -protein precursor (APP), 558 Anti-Aß monoclonal and  $\beta$ -secretase, 554, 572 antibodies (mAb), 564 and y-secretase, 556 Antianginal agents, 444 and  $\alpha$ -secretase, 571-72 Antiarrhythmic agents, 444 and v-secretase inhibitors. Antiarrhythmic drugs, 445 561 **Antibiotics** biology of, 548-49 and QT prolongation and the pathogenesis of potential, 444 reduced the number of Alzheimer's disease, 549

deaths, 464

Antibodies, 609

processing, 548-49

Swedish mutant, 555

and adeno-associated viral (AAV) vectors, 417 and diazeniumdiolates, 604 Anticancer agents and P-glycoprotein, 286 Anticoagulants risks with, 593 Anticonvulsants, 551 Antidepressants, 444 and attention-deficit hyperactivity disorder (ADHD), 271 and dopamine transporter (DAT), 528 in norepinephrine transporter (NET)-KO mice, 274, 275 Antifungal agents, 444 Antihistamines, 444, 447 Antihistaminics, 640 Antimalarials, 444 Antioxidant(s) and atherogenesis, 110 and calcium channel blockers (CCBs), 106 Antioxidant response element (ARE), 233-53 and cell signaling pathways, 246-52, 253 transcription factors acting on, 240-46, 251 Antipsychotic agents and Alzheimer's disease, 551 Antipsychotics, 444 Antipyrine, 13, 20, 21 and cigarette smoking, 18 oxidative metabolism of, 18, 19 Antiretroviral resistance and St. John's wort, 479 Antiretroviral treatment,

297-98

Antisense chimeras and cancers, 367 Antisense DNA ologomer, Antisense oligonucleotides, 154 and telomerase, 363, 366 Arrhythmias Aph-1 and y-secretase, 559, 560 Apolipoprotein (apo) A-I, 646-47 Apolipoprotein (apo) E and Alzheimer's disease, 549-50 ApoE4 Arsenic and  $A\beta$ , 572 and Alzheimer's disease, 549-50 and the blood-brain barrier, Arthritis 633 Apoptosis, 104 and cancer treatments, 202, 203, 207, 208, 213, 214, 217 cell death by, 362 and the dose-effect curve, 309-11 germ cell, 126, 134, 136, 138, 139 and Parkinson's disease. 532-33 Ascorbate and telemeres, 361 Apoptosis inducing factor (AIF), 534 Apoptosis specific protein (ASP), 533 Arachidonic acid, 84, 319-20 Arg16, 386, 388, 394 and asthma studies, 393 ASK1, 253 Arg64, 396-97 and \alpha\_2 adrenergic receptors Asp93, 555 (ARs), 402 Asp379 Arg296 residue of  $\beta$ -secretase, 554, 555 Arg389, 383, 385-86, 387, 390 Arg492, 398, 399 553 Aromatic amino acid

decarboxylase (AAAD) and C. elegans, 525 Aromatic hydrocarbons metabolic activation of, cardiac, 454 lethal, 112, 443, 453 risk of, 449 triggers, 443 Arrhythmogenesis mechanisms of, 449 and hormesis, 184 Arterial thrombotic disorders and nitric oxide (NO), 98 and oxidative stress, 253 Aryl-hydrocarbon receptor (AhR), 234, 235, 238, 250, 309-24 ligands, 309-24 signal transduction, Arvl-hydrocarbon receptor-nuclear translocator protein (ARNT), 234, 235 and nitrate tolerance, 101 Ascorbic acid and LDL oxidation, 110 and S-nitrosothiols, 101 synthesis, 5, 6 Asimadoline and P-glycoprotein, 639 Asn251, 399 of  $\beta$ -secretase, 554, 555 Aspartate, 558 Aspartic protease(s), 552, 553, 555 aspartic protease 2 (Asp2), inhibitors of, 555

Aspartyl proteases and Alzheimer's disease, 552 and presenilins, 558 Aspirin(s) compared to nitroaspirin, 104 development of, 464-65 and gastrointestinal toxicity, 102 nitric oxide (NO)-releasing, 103-4 Astemizole (Hismanol), 443, 444 Asthma, 151, 382 and adrenergic receptor polymorphisms (ARPs), 392-95 and S-nitrosothiols, 102 AT-1 antagonists and angiotensin converting enzyme (ACE) inhibitors, 107 Atenolol, 107-8 ATF4 protein, 246 Atherogenesis, 108 oxidation hypothesis of, and oxidative modification of LDL, 109 Atherosclerosis, 110 and Alzheimer's disease, and antioxidants, 111 and nitric oxide (NO), 98 Atherothrombotic disease, 109 ATP See Adenosine triphosphate Atria and cardiac electrical excitation, 441-42 Attention-deficit hyperactivity disorder

(ADHD), 261, 535

and dopamine, 270, 522 and dopamine transporter

(DAT)-KO mice, 271–72 Avidin and binding affinities, 37 and biotin, 39 Azimilide, 452 Azo dye N-demethylase induction of, 3–4 Azo-link reductase, 3–4 Azothioprine, 74

"Baby boomer" generation, 464 BACE1, 553 Bacteria and endotoxin, 610 and lipopolysaccharide (LPS), sensing, 611 Bacterial infection, 73 Barbital and CYP3A5, 164 and liver microsomal enzymes, 6 Basic region-leucine zipper (bZIP), 240-41, 245, 246, 247 Bayer Company, 465 Beef charcoal-broiled, 18

Behavioral symptoms in Alzheimer's disease, 551–52 Benadryl<sup>®</sup>, 6, 7

Benadryl<sup>®</sup>, 6, 7
Benz[a]anthracene

and human colon cell lines, 164 Benzamidine

Benzamidine modifies into parafluorobenzamidine, 35

Benzanthracene and human colon cell lines, 164 Benzimidazoles, 321–22

Benzo(a)pyrene (BaP)-DNA adduct, 155

Benzo[a]pyrene (BP), 5

and cytochrome P450, 11–12 enzyme induction by, 6–8 hydroxylation of, 13–14 and liver microsomal enzymes, 6

Benzo[a]pyrene hydroxylase and cigarette smoking, 17

Benzodiazepine L7, 452 Benzodiazepines, 551

7,8-Benzoflavone, 13–14 and xenobiotic metabolism, 20

Benzoquinoid ansamycins, 205

Benzphetamine and cytochrome P450, 11–12

Beta ( $\beta$ ) blockers, 107–8, 453 Beta-amyloid<sub>1–42</sub>

and blood-brain barrier functionality, 632

and P-glycoprotein, 637 Beta-carotene

and the Physicians' Health Study-II, 111

Bifunctional inducers explained, 235, 237, 238

Bilirubin (BR), 184, 318

Biliverdin (BV), 318 Binding affinities

and relaxed complex methods, 40-41

Binding affinity and free energy

calculations, 32–38 and semi-empirical linear response theory, 39

Biological thresholds belief in universality of, 177

Biologics Control Act of 1902, 466, 467

Biomarkers, 219 Biomedical devices

nitric oxide (NO)-releasing, 596

Biosensor accuracy, 597

Bioterrorism, 464 Biotin

and avidin, 39 Birfenidone, 79

Bladder tumor incidence and 2-AAF, 499, 500 and 4-ABP, 499

Bleomycin (BL)

and lung injury, 75–77, 84 Blood-brain barrier (BBB), 629–48

as an organ, 630, 631-32 and homeostasis and

disease, 632–33 methods to study transport, 633

transport processes at, 629, 631, 634-40

Blood pressure, 442 and Arg389, 387 and NCX-4016, 104 and PROLI/NO, 598 and sildenafil, 112 and single nucleotide polymorphisms, 99

polymorphisms, 99 Blood-testis barrier, 128–29

Blood vessels and diazeniumdiolates, 593–94, 595

BMS-214662, 216–17 Body fat distribution, 400

Borage

and lung disease, 85

Born model

and molecular dynamics simulations, 38

Botanical product(s) approval process, 471 bioavailability and bioequivalence of, 471 and financial incentives, 472

research on, 475-81 standardized, 476, 478

Bovine serum albumin (BSA), 105 Bradykinin, 106, 107

Brain	(JNK), 248, 249, 250,	Camptothecin, 209
of the Alzheimer's disease	253	Cancer Research
patient, 546	c-Kit, 136-37	page 450 of, 3
aneurysm, 598-99	c-MYC	Cancer(s)
drug transport to, 629-30,	and telomerase, 363-64,	and antisense chimeras,
631	369	367
tumors	CAAX, 215, 217	and aspirin, 465
and P-glycoprotein, 638	Cabbage, 19	cells
See also Blood-brain	Cadherins	and telomerase, 360,
barrier; Cerebral	and NMDA receptors	363, 369
vasospasm:	(NMDARs), 343	chemoprevention, 4, 5,
Cerebrovascular disease	Cadmium (Cd)	237
Breast cancer	at low doses, 191	colon
and CCI-779, 212	Caenorhabditis elegans,	and aspirin, 465
chemotherapy, 206	521-34	and MAPK, 212
and HER2, 205	apoptotic cell death	and epidermal growth
and miltefosine, 213	pathway in, 533	factor receptor (EGFR),
and R115777, 218	dopamine signaling in,	202
See also Cancer(s),	523-26	esophageal, 160
mammary	and dopamine transporter	and aspirin, 465
Brefeldin A	(DAT), 526-28	and hormesis, 183
and seminiferous tubule	and dopamine transporter	liver
fluid, 134	(DAT)-1, 529, 530-31	aminoazo dye induced,
Broccoli, 19	as a model system, 522-23,	3-5, 22
Brodie, Dr. Bernard, 5	536	mammary, 5
Bronchoalveolar lavage fluid	necrotic cell death in, 533	non-small cell lung cancer
(BALF), 77, 78, 79, 80,	Caffeine, 472	(NSCLC), 202, 203, 212,
84, 85	and cigarette smoking, 18	214, 217, 218
Brownian dynamics	metabolism of, 19, 21	ovarian cancer cells, 367
simulations, 38	Calcium (Ca), 335	and the Physicians' Health
Brussels sprouts, 19	Ca <sup>2+</sup>	Study-II, 111
Bryostatins	and cardiac electrical	risk assessment
and cancer treatments,	excitation, 442	governmental, 192
210-11	and PAF, 83	and hormesis, 188-89
Bupropione, 274	channel	risk due to
Bureau of Chemistry, 466	blockers, 105-6	N,N-diethylnitrosamine
Burns, Dr. John, 5-6	and dopamine, 528	(DEN), 497
Butachlamol, 525	modulators, 552	skin
1,3-Butadiene	Calcium/calmodulin-	and ozone pollution, 192
and carcinogenesis, 486	dependent protein kinase	stomach, 160-61
Butylated hydroxyanisole	II (CaMKII), 342,	and telomerase inhibitors,
(BHA), 236, 237, 241,	343-45	362, 367
245	Calcium calmodulin kinase	and therapeutic agents, 253
	and mammalian dopamine	therapy
C	transporters (DATs), 527	and P-glycoprotein
C225, 199, 207	Calmodulin, 344	inhibitors, 638
c-jun N-terminal kinase	Calreticulin, 62	treatments

dopamine receptor, 525

Cell(s)

signal See also Cancer(s): and nitric oxide (NO), 98 transduction-directed. Carcinogenesis; and the Physicians' Health 199-220 Carcinogen(s) Study-II, 111 and St. John's wort, 479 Carcinogen(s), 243 and red wine, 192 See also Breast cancer: bladder, 2-3 See also Cardiovascular chemical, 237 Carcinogenesis; disorders: Heart: Heart Carcinogenicity; and cigarette smoking, 17 failure (HF) and CYPs, 150 Cardiovascular disorders Carcinogen(s): Carcinoma(s); and diazeniumdiolates, 604 and nitric oxide Hepatocarcinogenesis: environmental (NO)-releasing drugs, 113 Hepatocarcinogens; human exposure to, 497 and S-nitrosothiols, 101 Leukemia(s): gastric, 161 See also Cardiovascular Lymphoma(s); and hormesis, 184 disease(s): Heart: Heart Melanoma; Tumor(s) low-dose linearity for, 177 failure (HF) Capase metabolism, 2 Cardiovascular medications and apoptosis, 533 and threshold mechanisms. and Alzheimer's disease. Carbachol, 108 487-91 573 Carbamazepine (Tegretol), and thresholds, 485-514 Carrier-mediated transport 551 tobacco-smoke, 159-60 (CMT) at the blood-brain barrier. Carbohydrates See also Cancer(s): 634 and diazeniumdiolates, 604 Carcinogenesis: in the diet, 18 Carcinogenicity Cartinoids, 320 and reactive nitrogen oxide Carcinoma(s) Caspase(s), 213 species (RNOS), 98 endometrial, 367 and C. elegans, 534 Carbon monoxide (CO), 8 heptocellular, 492 Catechol-O-methyl See also Cancer(s) and aminoazo dye transferase (COMT), N-demethylase, 10 Cardiac death 263 and hydroxylation of sudden, 449, 453 and C. elegans, 525 testosterone, 10 See also Coronary events; Catecholaminergic agents, and liver microsomes, 9 Heart failure (HF) 444 Carboplatin, 202 Cardiac function Catecholamine(s) and C. elegans, 524, 525 Carboxylesterase and angiotensin converting and exposure to vinvl enzyme (ACE) inhibitors, in norepinephrine acetate, 507 106-7 transporter (NET)-KO and the oral cavity, 512 See also Heart mice, 275 Carcinogenesis, 485-514 Cardiac transplantation list, Catenins, 343 chemical, 2 395 Caveolae and hormesis, 183 function of, 635 Cardiomyocytes and carcinogenesis, 490 CCI-779, 211-12 in nasal olfactory CD14 epithelium, 510 Cardiomyopathy sequence of events, 487 and adrenergic receptor receptor for polymorphisms (ARPs), lipopolysaccharide (LPS), See also Cancer(s); 386, 387, 403-4 612, 613, 615, 621 Carcinogenicity: Cardiovascular disease(s), cdc25C phosphatase, 210 Carcinogen(s) CeDOP1 Carcinogenicity 321

and deletion

polymorphism, 402

of vinyl acetate in rats and

mice, 501-6

cycle arrest and tumor incidence,	Cerebrovascular disease	and Alzheimer's disease, 572-73
487, 490	Cerebrovascular disease	and apolipoprotein (apo)
death	and chelation therapy, 471	A-I, 646–47
and Parkinson's disease,	See also Brain; Cerebral	and P-glycoprotein, 637
532–34	vasospasm	Choloroquine, 448
and telemeres, 361, 362	Cetuximab, 199, 207	Chromanol 293B, 452, 453
lines	cGMP, 97	Chromate
human colon, 164	and renin, 106	and nasal tumors, 151
natural killer (NK)	CGP57148B	Chromatin
and gene therapy, 429,	and cancer treatment, 199,	and retinoic acid receptors
430	200, 202, 219 CHAOS trial 111	and retinoid X receptors, 47, 52, 53–54, 55, 60, 63,
proliferation 400	CHAOS trial, 111	47, 32, 33–34, 33, 60, 63, 64
and carcinogenesis, 490 and tumor incidence,	Chelation therapy a study of, 471–72	Chromosomal aberrations,
and tumor incidence,	Chemical(s)	513–14
and vinyl acetate, 511,	carcinogenesis, 2	and acetic acid, 507
512, 513	environmental, 22	and vinyl acetate exposure,
senescence, 361, 362, 373	industrial, 151	508
signaling pathways	scanning, 41	Chromosome(s)
and the antioxidant	computational	end-to-end fusion, 361,
response element	experiments, 38–39	362, 369, 373
(ARE), 246-52, 253	Chemoprevention	and telomerase, 359
T cells	of cancer, 4, 5, 237	and telomeres, 360, 361-62
and gene therapy, 429,	Chemotherapy	Cigarette(s)
430	hormetic responses in, 186	and fetuses, 154
and telomerase, 359	Chloramphenicol acetyl	smoking, 22, 156
types	transferase (CAT), 238,	and CYP expression,
in the G.I. tract, 159	239, 241, 242	157
within the lung, 151	Chlorcyclizine	and drug metabolism,
more susceptible to	and cytochrome P450,	17–18
toxicities, 152	11–12	and lung cancer, 151,
Cellular death, 528	Chloride channels	156
Cellular retinoic acid binding	and P-glycoprotein, 637	See also Smokers; Tobacco
proteins (CRABPs), 58	Chloroform	smoke
Central nervous system	and CYP genes, 156	Circadian rhythm, 317
(CNS)	7-Chlorokynurenic acid,	Circum-ventricular organs
diseases, 633, 635	644	(CVOs), 631
disorders	Chlorpromazine	Cisapride (Propulsid), 444, 448
drug therapy for, 640	and C. elegans, 525 Chlorthion, 8	Cisplatin, 202, 206, 207
and HIV, 639 Cephalic cells (CEPs)	Chlorzoxazone, 6, 7	Clara cells, 151–52
and C. elegans, 523	oxidative metabolism of,	Claritin, 443, 444
Cerebral vasospasm	19	Clathrin, 634
and diazeniumdiolate	Cholera	Cleaning agent, 126
therapy, 601	resurgence of, 464	Clinical studies
See also Brain;	Cholesterol	informed consent to, 466
,		

and St. John's wort, 479

and grapefruit juice, 162

Cyclosporine, 294, 296-97

**CYPs** 

Clinical trials accumulation of, 73, 74, See also Cardiac death: and botanical products, 77, 80, 81, 85 Heart: Heart failure (HF) 474-75, 478 synthesis, 84 Coronary heart disease and cancer treatments, 219 and TGF-B, 77 (CHD) Clofibrate, 8, 12 and nitric oxide (NO), 98 Clotrimazole cancer and sildenafil, 112 and CYP3A5, 164 and statins, 109 and aspirin, 465 and drug metabolism, 16 and MAPK, 212 therapy for, 99 Clozapine, 270 cell types in, 159 See also Coronary artery Coactivator-associated cytochrome P450 in, 151. disease: Coronary arginine 163-64 atherosclerosis; Heart; methyl-transferase I Complementary and Heart failure (HF) (CARMI), 58-59 alternative medicine Coronary stenoses Cocaine (CAM), 463-82 and L-arginine, 110 and dopamine transporter Computational experiments Corticosteroids, 74 (DAT), 267, 268-69, 526, Coumarin, 13, 236, 237, 238, chemical-scanning, 38-39 528, 531, 535 Computer technology 241 and dopamine transporter and drug design, 31-32, 41 and CYP genes, 156 (DAT)-KO mice, 268-69, Congophilic amyloid and the esophagus, 160 270, 272 angiopathy (CAA) and grapefruit juice, 162 in mutant mice, 277 and Alzheimer's disease. Cranberry in norepinephrine 547, 549 research, 476 transporter (NET)-KO Contraceptives CREB binding protein (CBP) and St. John's wort, 479 CBP/p300, 53, 54, 55, 58 mice, 274, 275 Crohn's disease (CD), 299 in serotonin transporter Copper (Cu) and S-nitrosothiols, 101 (SERT)-KO mice, 273 Cryptogenic fibrosing Codeine Corn oil (CO) alveolitis, 73 demethylation of, 8 and lung disease, 85 See Idiopathic pulmonary Cognitive decline Coronary artery fibrosis and Alzheimer's disease. nitric oxide (NO) delivery C3435T to, 591-92 polymorphism of MDR1, 546 Cognitive deficits See also Heart 293-94, 295, 296, 299 and Alzheimer's disease. Coronary artery disease **Current Good Manufacturing** 546 and balloon angioplasty, Practice (CGMP), 466, Cognitive functions 468, 470 and blood-brain barrier and chelation therapy, 471, Cyclin-dependent kinases functionality, 633 472 (CKDs), 208, 209, 210 Colchicine, 74 See also Coronary Cycloheximide, 385 and seminiferous tubule atherosclerosis; Coronary Cyclooxygenase-2 (COX-2), fluid, 134 heart disease (CHD): 85, 102 and spermtogenesis, 140 Heart; Heart failure (HF) Cyclophosphamide, 74, 206 Coronary atherosclerosis, 111 Cyclosporin ulcerative colitis (UC), See also Coronary artery and drug metabolism, 16

> disease; Heart Coronary events

> > polymorphism, 402

and deletion

299-300

Collagen, 86

biosynthesis, 74, 75

Collaen

in fetal tissues, 154	and the G.I. tract, 160, 161,	and the respiratory tract,
in human nasal mucosa,	162, 163, 164	152
151, 152	and P-glycoprotein, 288	CYP2E1, 149, 488
CYPIA	and the respiratory tract,	and the G.I. tract, 160, 161,
and the G.I. tract, 160, 161,	152, 154, 157	164
162, 163, 164	CYP3A5, 149	and the respiratory tract,
CYP1A1, 149, 234, 237, 238	and the G.I. tract, 160, 161,	152, 154, 155, 156, 157
and the aryl-hydrocarbon	162, 163, 164	CYP2F, 157-58
receptor (AhR), 310, 313,	and the respiratory tract,	CYP2F1, 149
316, 318, 319, 320, 321,	152, 156, 157	and the G.I. tract, 161
323	CYP3A7	and the respiratory tract,
in the respiratory tract,	and the G.I. tract, 161	152, 153, 154, 157, 158
152, 154, 155, 156-57	CYP4A	CYP4F12
and tryptamine, 317	and the G.I. tract, 160,	and the G.I. tract, 162
CYP1A2, 149	164	CYP2G
and the aryl-hydrocarbon	and the respiratory tract,	and the respiratory tract,
receptor (AhR), 318	152	152
and the G.I. tract, 160, 161,	CYP1B1, 149	CYP2G1, 156
163	and the G.I. tract, 161, 163,	CYP2G1, 153
and the respiratory tract,	164	Cyp2g1 gene, 158
152, 155, 156, 157	and the respiratory tract,	CYP2J
CYP2A, 157-58	152, 154, 156, 157	and the respiratory tract,
and the respiratory tract,	CYP2B	152
153	and CYP induction, 157	CYP2J1, 149
CYP2A3, 158	and the G.I. tract, 164	and the respiratory tract,
CYP2A5, 156	CYP2B, 157-58	152–53
Cyp2a5, 158	CYP2B6, 149	CYP2J2, 149
CYP2A6, 149	and the G.I. tract, 161	and the G.I. tract, 160, 161,
and the G.I. tract, 160, 161	and the respiratory tract,	162, 163
and the respiratory tract,	152–53, 154, 157	and the respiratory tract,
152–53, 154, 155, 156,	CYP2B7P, 153	152, 154
157	CYP4B1, 149	CYP2S1
CYP2A7	and the G.I. tract, 160, 161	and the G.I. tract, 161, 162
and the small intestine, 161	and the respiratory tract,	and the respiratory tract,
CYP2A7, 153, 157	152, 154, 157, 158	153–154
CYP2A13, 149	CYP2C, 152, 157, 159	Cys492, 398
and the respiratory tract, 152–53, 154, 155, 156,	and the G.I. tract, 161, 162, 164	Cysteine, 215, 235, 252, 253 pro-drugs
157	CYP2C8, 149	and lung fibrosis, 86, 87
CYP3A, 159, 160	CYP2C9, 149	Cystic fibrosis
and the G.I. tract, 163, 164 and the respiratory tract,	and the G.I. tract, 162 CYP2C18, 149	transmembrane regulator protein (CFTR), 637
152, 154	CYP2C19, 149	Cytochrome P448, 11, 12
and St. John's wort, 479	and the G.I. tract, 162	Cytochrome P450 (CYP), 1,
CYP3A3	CYP2D6, 149	3, 7, 8, 11, 14, 16, 100,
and the G.I. tract, 163	and the G.I. tract, 159, 161	149–65, 603
CYP3A4, 149, 296, 297	CYP2E	activation of, 16
0 11 5/17, 177, 270, 277	~	

491-92, 493

7,8-Dihydrodiol, 13

and the aryl-hydrocarbon Dementia and polymorphisms, 396 receptor (AhR), 319 AIDS, 639 Diabetic men in the colon, 151, 163-64 and Alzheimer's disease, and erectile dysfunction, and environmental factors. 546, 551, 552, 573 and the blood-brain barrier. Diacylglycerol, 213 in the esophagus, 151, 632 Diastole, 442 159-60 Diazenium diolates, 585-605 Deoxycholate explained, 9 and aminoazo dye diazeniumdiolated metal in the gastrointestinal tract, N-demethylase, 10 surfaces, 592-93 150, 151, 158-64 Deoxycorticosterone, 8 and erections, 601, 602 Department of Agriculture, and liver microsomes, 9-13 ionic, 586-89 and microsomal 466 structure, 586, 587 metabolism, 154-55 Dependoviruses, 414 and toxicity, 603-4 in the respiratory tract, Depolarization 2,6-Dichlorobenzonitrile 150, 151-58, 164 cardiac and CYP genes, 156 in the small intestine, 151, and HERG channels, and CYP2A13, 153 161 - 63445 5,7-Dichlorokynurenic acid, solubilization and and cardiac electrical purification of, 10-13, 22 excitation, 442 Diclofenac, 16, 105 in the stomach, 151, diastolic, 452 Diet 160-61 Depression, 261 and arvl-hydrocarbon Cytochrome P450 reductase and Alzheimer's disease, receptor (AhR) ligands. (CPR), 159 313-15 and St. John's wort, 481 and cancer risk, 238 Cytokine IL-1, 614 Cytokine release Desipramine effects on drug and NCX-4016, 104 and dopamine transporter metabolism, 18-20 Cytokines, 617 (DAT)-KO mice, 269 Dietary Supplement Health and ILF, 77-82, 83, 85, 87 in norepinephrine and Education Act Cytoplasmic dyneins of 1995, 467-68 transporter (NET)-KO and microtubules, 132-33, mice, 274 Dietary supplements Deskar®, 79 134 legislation for the Cytotoxicity DETA/NO. 587, 588 regulation of, 467 and carcinogenesis, 490, requirements for, 468-72 in angioplasty treatment, 509, 510, 511 591-92 and structure/function and HSV-1 vectors, 429 claims, 468 and cerebral vasospasm, and nitric oxide (NO), 98 598-99 Diethyl maleate, 235, 236 and tumor incidence, 496 and pulmonary Diethylenetriamine/NO, 104 and vinyl acetate, 512, 513 hypertension treatment, Digitalis, 466 Cytotoxin 600 - 1Digoxin, 286, 287, 288 and nitric oxide (NO), 98 Detoxification and heart failure, 466 enzymes, 323 Dihomo gamma linolenic acid (DGLA), 85 D in the smalll intestine, 161 8,9-Dihydro-8-(N7 guanyl)-9-DAPT Devalproex sodium (Depakote), 551 hydroxyaflatoxin B1 -secretase inhibitor, 561, 562 Dexamethasone, 12 (AFB1-N7-Gua) adduct,

Dextromethorphan, 21

Diabetes

**DEA/NO, 588** 

Decorin, 81

1,4-Dihydropyridine calcium channel blockers (CCBs), 105 Dihydroxyphenylacetic acid (DOPAC) and C. elegans, 524, 525 ν-Diketone neurotoxicity, 129 Diltiazem and tacrolimus, 639 Dimethyl sulfate and BL-induced lung fibrosis, 76 7.12-Dimethylbenz[a]anthracene, Dioxin, 8, 12 and the arvl-hydrocarbon receptor (AhR), 309, 310, 311, 313, 316, 317-18, 319-20, 321 and hormesis, 184 at low doses, 191 Dioxin responsive element (DRE), 310, 318 Diphenhydramine, 6, 7 Disease(s), 386 and  $\beta_2$  adrenergic receptor (AR), 392 and adrenergic receptor polymorphisms (ARPs), 386, 404 and the blood-brain barrier. 632-33 chronic, 464 incidence decreased, 177 and mutation, 382 and nitric oxide (NO), 98 orphan, 472 and oxidative stress, 253 susceptibility, 298-300 1.2-Dithiole-3-thione and the antioxidant response element (ARE),

235, 237, 238

Diuretics, 444

hypokalemia due to, 449 DMAEP/NO, 588 and pulmonary hypertension treatment. 600 - 1DNA adduct(s) and carcinogenesis, 495, 496, 497, 498, 499 and adeno-associated viral (AAV) vectors, 414-15, 416-17 and adenoviral vectors, 424, 426 damage, 362, 487, 488, 490, 491 and aflatoxin B1, 491 and urban pollution, 151 end replication problem. and exposure to vinyl acetate, 507-8 and gene therapy, 413 and HSV-1, 427, 428, 429 and oncoretroviruses, 423 repair, 487, 488-89, 490 and styrene oxide, 488 and telomeres, 361 telomeric, 359, 360, 361, 362, 367, 368, 371 DNA binding domain (DBD) and nuclear receptors, 49-50 Docetaxel, 202, 207 Dodson, John, 185 Dofetilide (Tikosyn), 444, 445, 446, 447, 448 Donepezil (Aricept) and Alzheimer's disease. 551 DOPA decarboxylase, 277 DOPAC, 528 Dopamine (DA) in C. elegans, 523-26 dopamine transporter(s) (DAT), 261-62

and C. elegans, 523-26, 529, 530-31 dopamine transporter knockout (DAT-KO) mice, 262-72, 273, 275, 276-77, 278, 526-27 dopamine transporters (DAT)-1, 529, 530-32 mammalian and C. elegans, 526-28 and Pakinson's disease. 528-30, 535 and Parkinson's disease (PD), 521, 522, 527, 528-30, 535 Dose-effect curve and carcinogenesis, 485. 487, 488, 490, 491, 494, 495 relationships, 499 Dose response(s) biphasic, 185 dose-response curve(s) and genotoxic carcinogens, 499 of vinyl acetate, 501 dose-response relationship(s) biphasic, 186 and genotoxic chemicals, 513 and the hormetic paradigm, 189-91 for N,N-diethylnitrosamine (DEN), 497 U-shaped, 180, 181 and the Yerkes-Dodson Law, 185 hormetic, 179, 193 hormetic biphasic, 182, 183 models, 184 paradigms, 176 revolution, 176-77, 193

and risk assessment. nitric-oxide releasing. wood 188-89 97-114 Doxorubicin, 202, 206, 207, number one, 465 211 orphan, 466-67 Droperido, 525 oxidative metabolism of, Drosophila, 614, 622 Dystonia Drosophilia melanogaster, and P-glycoprotein, 613 637-40 Drug(s) with QT-prolonging E abuse, 261 potential, 444 addiction regulation in the U.S., and dopamine, 522 466-72 and the blood-brain barrier. requirements for, 468-72. 629-48 478 Edema and cardiac K+ channels, stages in development of, 474-75 over the counter (OTC). that block HERG, 447 that interfere with therapy, 471-72 requirements for. monoamine transporters, 468-70, 478 278 standards, 468 that modify behavioral and CYPs, 150 symptoms in Alzheimer's disease, 551-52 delivery and the nose, 152 transported by 442 P-glycoprotein, 286, computer-aided, 31-41 287-88, 296-97 drug-drug interactions and Drug metabolism, 630 P-glycoprotein, 288 activation of, 14-16 drug-metabolizing and cigarette smoking, enzymes, 1-22 17 - 18effects on drug CYP-mediated, 150 metabolism, 16-20 effects of diet on, 18-20 enzyme induction by, 5-6 effects of drugs on, 16-20 and financial incentives. induction and inhibition of. 632 472 16 - 20glutamatergic intraindividual variability and dopaminergic in. 20-22 Drug Price Competition and hyperactivity, 270 Patent Term Restoration hydroxylation of, 12 and ILF, 73 Act (Waxman-Hatch interactions with Act) Endosomes complementary and of 1984, 467 alternative medicine **Durham-Humphrey** (CAM), 478-80 Amendments

of 1951, 466, 467

inhalation of, 73

Dust(s)

legislation for the

regulation of, 467

neuroprotective, 536

and nasal tumors, 151 Dynamin, 634 Dyslipoproteinemia and polymorphisms, 396 and C. elegans, 525 E-4031, 445, 446 Echinacea, 476 research on, 476, 477 Edelfosine, 212-13 and nitric oxide (NO), Edetate (EDTA) chelation

EGFR-TK, 203 Eicosanoids, 84-85 Electrical excitation cardiac, 441-42 Electrocardiogram (ECG), Electrocardiographic

abnormalities, 441, 442, 449, 454 Electrophile response element (EpRE), 238 Embryogenesis, 48 Enalapril, 107 Encephalitis and the blood-brain barrier,

Endocytosis, 634-35 Endoplasmic reticulum (ER) endoplasmic reticulum/Golgi, 348 and NMDA receptors

(NMDARs), 338-39 and NMDA receptors (NMDARs), 341 Endothelial dysfunction

and nitric oxide (NO), 98 **Endothelial function** 

and angiotensin converting

cancer risk assessment, 188 Equine infectious anemia enzyme (ACE) inhibitors, and kidney tumors, 177 virus, 423 106 - 7**Environmental toxicity** Erectile dysfunction and L-arginine, 110 and the respiratory tract, in Carl Djerassi's novel, and statins, 109 586 and vitamin E, 111-12 151 Enzyme(s) therapy, 112-13 Endothelial nitric oxide and  $\beta$ -secretase, 552 treatment of, 603 synthases (eNOS), 100, See also Erection(s) azo dye-metabolizing, 3-5 101 beta-site APP-cleaving Erection(s) and angiotensin converting enzyme (BACE), 553 erection-inducing drugs, enzyme (ACE) inhibitors, 601, 603 107 and C. elegans, 525 cytochrome P450, 149-65 penile and calcium channel blockers (CCBs), 106 detoxification, 323 and nitric oxide (NO), 98 and oxydized low-density detoxifying, 488 See also Erectile lipoprotein, 109 DNA repair, 489, 490 dysfunction drug-metabolizing, 1-22, ERG1, 445 and statins, 108, 109 ERK1, 212 Endothelial vasomotor 233-53 ERK2, 212, 248 function, 111 induction Endothelin-1, 106, 107 by benzo[a]pyrene, 6-8 Erlotinib, 199, 203 Endotoxin(s) by drugs, 5-6 Erythromycin, 444, 447 and grapefruit juice, 163 hematopoietic cells, 612 and polycyclic aromatic Esophageal cancer, 160 hydrocarbons, 3-5 receptor signal transduction from. by xenobiotics, 234. and aspirin, 465 616-17 235-38 Esophagus the term, 610 and organic nitrate esters, cytochrome P450 in, 151, tolerance, 617 100 159 - 60telomerase, 359-74 Essinophilic granuloma, 73 and Toll-like receptors, 609-22 xenobiotic metabolizing. Estradiol, 8 and cigarette smoking, 17 Environment 309, 310, 323 and drug metabolism, 20, Ephedrine alkaloids, 472 hydroxylation of, 17 Epidemiological studies Estrogen 21 - 22Environment regulatory of vinvl acetate and St. John's wort, 479 carcinogenicity, 506-7 Estrone, 8, 17 agencies Epidermal growth factor Ethane dimethane sulphonate and hormesis, 188 receptor (EGFR), 202, (EDS) Environmental agents and testicular atrophy, and Parkinson's disease, 203, 205, 207 535 Epinephrine, 393, 394, 399, 138 - 39Ethanol, 8, 12 Environmental clean up 401, 403, 444 standards, 192 and adrenergic receptors and drug metabolism, 16, Environmental contaminants, 19-20 (AR), 381 309 Epirubicin, 206 Ethinylestradiol Environmental health Epithelial lining fluid (ELF) and grapefruit juice, 162 dogmas, 191 and pulmonary fibrosis, 85 Ethionine, 10 Environmental issues **Epoxide** Ethnic groups and public media, 192 genotoxic, 488 MDR1 genetic variants in, **Environmental Protection** 289-91, 293-94 Epstein-Barr virus Agency (EPA) and HSV-1 vectors, 429 7-Ethoxycoumarin, 13, 19

scavengers

Ethoxyquin, 236, 237, 241 and drug and dietary Fluid phase-mediated Ethylnitrosourea, 490 supplement requirements. transport (FMT) Etoposide, 202 468-70, 471 and the blood-brain barrier. Evening primrose oil (EPO). present day, 466 Federal Food, Drug, and 5-Fluorouracil (5-FU), 209 Excitatory post-synaptic Cosmetic Act Fluoxetine currents (EPSCs). of 1938, 466, 467 and dopamine transporter 345-46, 348 Federal Trade Commission (DAT)-KO mice, 270 Exercise and claims in advertising. Foamy viral (FV) vector(s) and polymorphisms, 387. 468 and gene therapy, 418, Feline immunodeficiency 421-23 virus (FIV), 423 Extracellular matrix (ECM) properties of, 431 proteins, 73, 75, 77, 78, Felodipine, 19 Foamy virus, 414 82, 85 and grapefruit juice, 162 Folate Extracellular regulated kinase Fenamate, 453 and nitrate tolerance, 101 (ERK), 247, 248, 249, Fetal tissues Foods 250 CYPs in, 154 manufacturing Extracorporeal membrane requirements for, 468 oxygenation (ECMO) agent responsible for, 610 safety of, 466 circuits Fexofenadine Forearm blood flow (FBF) and diazeniumdiolates. and P-glycoprotein, 287, and beta  $(\beta)$ -blockers. 594, 596 296, 297 108 Eye diseases Fibroblast growth factor Formaldehyde-induced and the Physicians' Health (FGF), 204 florescence (FIF) Fibroproliferative diseases, 77 and C. elegans, 524 Study-II, 111 Filovirus (Ebola Zaire), 422 6-Formylindolo(3,2b)-Financial incentives carbazole (FICZ) Fabric printing workers and botanical products, 472 and arvl-hydrocarbon and polyneuropathy, 126 in the development of receptor (AhR) ligands, Farnesyl protein transferase drugs, 466-67, 472 316, 317 (GTT), 215 Five-year survival, 387 Foxglove Farnesyl transferase Flavone, 13, 14-15 extracts of, 465-66 inhibitors, 199, 215-18 Flavonoid(s) Free energy calculations Farnesylpyrophosphate and the antioxidant and drug design, 31, (FPP), 215 response element (ARE). 32-38, 41 and statins, 108-9 237, 250 and the  $\lambda$  dynamics Fas system, 139 and aryl-hydrocarbon method, 33-34 and Sertoli cells, 136 receptor (AhR) ligands, and locally enhanced Fat 313 sampling (LES) method, body fat distribution, 400 inhibit CYP3A4, 162 in the diet, 18 and multiple and solvent models, 36-38 mass, 402 monooxygenases, 13-14 and Zwanzig's perturbation Flavopiridol, 199, 207-9 Fatty acid theory, 35-36 polyunsaturated Flecainide, 448 Free radical(s) and lung disease, 85, 87 Flesinoxan, 639 and Parkinson's disease. Federal Drug Administration Flexin, 6, 7 529

Flk1/KDR, 204

(FDA)

and Alzheimer's disease. neuroprotective strategy, gene) 550 Genetic screen 552 and the antioxidant forward, 531-32 Fruits Geranylgeranylpyrophosphate and aryl-hydrocarbon response element (ARE), receptor (AhR) ligands, 233-53 (GGPP) CYP and statins, 108-9 and cancer risk, 238 and the G.I. tract. Germ cell(s) 158-64 alterations in, 134 G and the respiratory tract, apoptosis, 126, 134, 136, y-Aminobutyric acid 138, 139 152 - 58(GABA) defects c-kit. 137 and cardiac arrhythmias, depletion of, 134 GABAB receptors and the endoplasmic 453-54 maturation, 133 and Sertoli cells, 128-29, reticulum, 339 delivery systems and gene therapy, 135, 140, 141 G-quadruplex(es) and c-MYC expression, 413-14 Ginkgo biloba, 479, 481 and drug metabolism, 20 364 Ginseng, 476 expression, 310-11 and telomeres, 368, GISSI-Prevenzione trial, 111 371-72, 373 arvl-hydrocarbon BGlc-PYRRO/NO, 589, 604 GLEEVEC® G-tetrads, 368 receptor GABA (AhR)-dependent, 312, and cancer treatment, 199. See y-Aminobutyric acid 313, 314, 315, 316, 200, 202, 219 Glu 317, 319, 320, 321, (GABA) deleted, 400-1 Galantamine (Reminyl) 322, 323 Glu27, 388, 389 and Alzheimer's disease, **hTERT. 363** 551 and nuclear receptors, and hypertension, 395 Gamma-linolenic acid 48, 61, 63 and obesity, 396 (GLA), 85, 87 and familial Alzheimer's Glucocorticoid cortisol Gastrointestinal stromal disease, 545, 549-50 and P-glycoprotein, tumors (GIST), 202 gene-dose effect 636-37 Gastrointestinal toxicity and dopamine Glucocorticoid receptor transporter expression, and nitric oxide (GR), 55, 56 (NO)-aspirin, 104 Glucocorticoid receptor and nonsteroidal interacting protein ras anti-inflammatory drugs and cancer treatments. (GRIP1), 55 Glucocorticoids, 86 (NSAIDs), 102 215 Gastrointestinal tract therapy, 114, 413-32 Glutamate cytochromes P450 in, 150, viral delivery systems in C. elegans, 523 151, 158-64 explained, 413-14 and NMDA receptors with viral vectors, (NMDARs), 336 and vinyl acetate exposure, 511 413-32 receptors, 350 GBR 12909 transcription Glutaraldehyde and dopamine transporter and retinoids, 47, 52, 53, microtubules treated with. (DAT), 528 133-34 Glutathione (GSH), 85-86, Geldanamycin, 205 tumor suppressor, 199 Gemcitabine, 207, 209 See also HERG (human 237, 245, 641 Gly16, 388, 389, 393, 394 ether-a-go-go-related Gene(s)

and asthma studies, 393 and hypertension, 395 Glv49, 382, 383, 384-85, Hantavirus, 464 386, 387 Gly389, 383, 385-86, 387, 394, 404 390, 404 Hazard Gly648, 448 assessment, 192 Glyceryl trinitrate, 99 186-87 Glycine, 336 Glycoproteins and HSV-1 virus, 428 and retroviruses, 422 process of, 175 Gonadotropin releasing Health hormone (GnRH) and testicular atrophy, 138 Government toxicological agenda, 176 (CAM), 463 Governmental agencies and established paradigms, effects Governmental cancer risk 187 assessment, 192 Heart GR 127935, 274 390, 395 Grapefruit juice, 19, 162-63, 165 attack Green fluorescent protein disease and dopamine transporter (DAT), 528, 529 114 GTP cyclohydrolase and IKr, 445-49 (GTPCH) and C. elegans, 525 rate, 390 Guanine and AFB1 epoxide, 491 Guanine nucleotide binding proteins (G-proteins), 381 3'.5'-Guanosine monophosphate (cGMP), 601 Guanylate cyclase, 97 and CYP3A4, 164 H

Halogenated aromatic hydrocarbon (HAH), 309, 311–12 Haloperidol, 270, 525, 551 disease (CHD): Heart and C. elegans, 525 failure (HF); Myocardial infarction (MI) Haplotypes, 387, 390-92, Heart failure (HF) and  $\beta_1$  adrenergic receptor polymorphisms (ARPs), and hormesis, 184, and  $\beta_2$  adrenergic receptor polymorphisms (ARPs), and regulatory agenicies, and adrenergic receptor polymorphisms (ARPs). of the American people, after myocardial infarction (MI), 107 and complementary and and digoxin, 466 alternative medicine and nitric oxide (NO), 98 and stroke volume, 100 See also Cardiac death: beneficial and adverse. Coronary events: Heart Heat shock protein 90, 205, 310 and  $\beta_2$  adrenergic receptor, Helmholtz free energy and solvent models, 37-38 and Zwanzig's perturbation and aspirin, 465 theory, 32-33, 35 Help virus and inhaled nitric oxide, and Ad vectors, 425 Hematopoietic cells how it works, 441-42 and endotoxin sensing, 612 Heme complexes and the antioxidant and Arg389, 387 response element (ARE), sudden increases in, 454 235 transplant rejection Hemophilia B and St. John's wort, 479 and gene therapy, 430 See also Cardiac death: Hepatic drug metabolism, 5 Cardiac function; Cardiac Hepatocarcinogenesis transplantation list: aflatoxin B1-induced, 238 Cardiovascular disease(s); See also Cardiovascular disorders: Hepatocarcinogens; Liver Cardiovascular Hepatocarcinogens, 603-4 medications; Coronary See also artery; Coronary artery Hepatocarcinogenesis; disease; Coronary HER2 atherosclerosis; Coronary

events; Coronary heart

and cancer, 205-6, 207

and adeno-associated viral

(AAV) vectors, 414-15

Hexamethylphosphoramide Hormone nuclear receptors, Herbal medicines and safety and efficacy, (HMPA) 47-64 and CYPs, 153, 155, 156 Hsp90 protein, 363 480-81, 482 2,5-Hexanedione (2,5-HD) HSV-1 See also Herbal products; Herbal remedies See Herpes simplex virus exposure and germ cell death, 136 Herbal products, 315 type 1 (HSV-1) microtubules treated with. and drug interactions. **hTERT** 475-76, 478-80 133 - 34and telomerase, 359, 360, 363, 365, 367, 369, 374 See also Herbal medicines; and testicular injury, 125-41 Herbal remedies hTR Herbal remedies, 22 Hexobarbital, 7, 13 hTR RNA template, 359, and prescription drugs, 16 High-throughput screen 363, 365, 367 and telomerase, 359, 360, See also Herbal medicines: (HTS), 535-36 Herbal products Hippocrates, 464, 465 humAb4D5, 206 Herbicides Histamine Human antimurine antibodies and hormetic effects, 186 and C. elegans, 524 Herbimycin, 205 Histone acetyl transferase (HAMA), 206 Herceptin, 199, 205-7 (HAT), 52, 53, 54, 55 Human immunodeficiency HERG (human Histone acetylation virus (HIV) and coactivators, 63 and inhibitor binding ether-a-go-go-related gene), 443 Histone deacetylase(s) affinity, 39 and MDRI channels, 445 (HDAC), 52 and IKr current, 445-46 and corepressors, 63 polymorphisms, 297-98 HIV and P-glycoprotein at the IKr/HERG blockade, blood-brain barrier, 639 446-49 See Human immunodeficiency virus Human immunodeficiency K+ channels, 443, 445, 446-49 (HIV) virus type 1 (HIV-1) and methanesulfonanilides, HMR 1275, 199, 207-9 integrase, 40 and lentiviruses, 419-21, 448 Holoenzyme vestibule, 448-49 tolemerase, 359-74 Herpes simplex virus type 1 Homovanillic acid Human immunodeficiency (HSV-1) and C. elegans, 524 virus type 2 (HIV-2), 423 structure and replication. HOPE trial, 111 Huntington's disease, 534 427-28 Hormesis, 175-93 Hydralazine acceptance of, 176-77 and nitrate tolerance, 101 vector(s) development and evidence of, 177-84 Hydrocarbons production, 428 impediments to acceptance and BP hydoxylase, 5 properties of, 431 of, 191-92 and enzyme induction, 22 legal implications of, 192 polycyclic tropism and transduction, 428-29 in non-toxicological fields, and azo dye Herpes simplex virus type 1 185-86 carcinogenesis, 3-5 not seen too often, 177 and charcoal-broiled (HSV-1) vectors and risk assessment, beef, 18 and gene therapy, 414, 427-29 and enzyme induction, 6, 186-92 Herpes virus Hormetic hypothesis

mechanism argument

against, 182

polycyclic aromatic

hydrocarbons

and enzyme induction, and nebivolol, 108 (DAT), 528 3-5 and nitric oxide (NO), 98 Immune system and xenobiotic pulmonary responses to microbial metabolism, 17-18 and inhaled nitric oxide. poisons, 609-22 Hydrogen peroxide, 528, 529 114 Immunity 1-Hydroxy-2-aminoand sildenafil, 113 two types of, 609 naphthalene, 2-3 and single nucleotide Immunotherapy 15-Hydroxyelcosatrienoic polymorphism (SNP), 99 for Alzheimer's disease. (15-HETrE) acid. 85 treatment of, 105 564-71, 573 Hydroxyl radical Hypertrophy Impotence and Parkinson's disease, and adrenergic receptor treatment of, 112 528, 529 polymorphisms (ARPs), See also Erectile Hydroxylation, 6, 7 399 dysfunction of benzo[a]pyrene, 13-14 Hypochlorous acid (HOCl) Incontinence and liver microsomal fatty and BL-induced lung and adrenergic receptor acid, 10-11 fibrosis, 76 polymorphisms (ARPs), of testosterone, 8-10, 22 399 Hypocholesterolemic agents, of zoxazolamine, 14-15 444 Indapamide, 452 Hydroxymethylglutaryl Hypokalemia, 449 Indigenous peoples, 464 (HMG)-CoA reductase Hypotension Indigo, 317, 318 inhibitors, 108-9 Indinavir, 297 postural, 298 5-Hydroxytryptophan and St. John's wort, 479 ï (5-HTP) Indirubin, 317, 318 Ibuprofen and C. elegans, 525 Indole acetic acid, 316, 317, and dopamine transporter and AB42, 563-64 321 (DAT)-KO mice, 270 Ibutilide (Covert), 444, 446 Indoles, 316-18 Hyperactivity Idiopathic pulmonary fibrosis and human colon cell lines. and dopamine transporter (IPF), 73-87 164 (DAT)-KO mice, 269-70, and pirfenidone, 79 Indomethacin IKr, 443, 445-49 271, 272 and A842, 563-64 in mice, 273 blockade, 449 Infection(s), 618, 620 Hypercholesterolemia role in the heart, 445 and echinacea, 476 and L-arginine, 110 Iks, 443, 445, 450-54 fungal Hyperdopaminergia autonomic regulation of, and flies, 614 in dopamine transporter 451-52 gram-negative, 611, 618 (DAT)-KO mice, 269-71 blockade, 452 immune responses to, 610 Hyperforin IL-1, 83 Infectious diseases and drug metabolism, 16  $IL-1\alpha$ , 79 and S-nitrosothiols, 102 Hypertension, 107, 382, 395 IL-6, 83 Inflammation, 74, 612 and adrenergic receptor Ile164 lung, 80 polymorphisms (ARPs), polymorphism, 388, 389, and lung fibrosis, 85 399, 400 390, 395 Inflammatory bowel disease and Arg389, 387 Imatinib mesylate and MDRI and the blood-brain barrier. and cancer treatment, 199. polymorphisms, 299-300 632 200, 202, 219 Inflammatory cells, 77-83 and deletion **Imipramine** Inocula, 618-20

and dopamine transporter

Insulin secretion, 402

polymorphism, 402

Integrins and ILF, 82-83, 87 and neurons, 346 Interferon gamma (INF-y), 80-81 Interleukin-6 (IL-6) and Bryo 1, 211 and NCX-4016, 104 Internet and complementary and alternative medicine (CAM), 464 Ion channels cardiac, 441-42 Ioratadine (Claritin), 443, 444 Ipsapirone, 274 IRAK gene and LPS, 616 IRAK4 gene and LPS, 616, 621, 622 Iressa and cancer treatment, 199, 202 - 3Irinotecan, 209 and St. John's wort, 479 Iron (Fe) and the brain, 644-45 and dopamine, 528, 529 Ischemia and nitrate, 100 Isoniazid, 12 Isoproterenol and adrenergic receptor polymorphisms (ARPs), 384, 385, 388 and Iks blockers, 453 Isosafrole, 8, 12 and CYP3A5, 164 Isosorbide 5-mononitrate, Isosorbide dinitrate, 99 Isosorbide mononitrate, 112 Kinins Isothiocyanate(s), 235, 236, 238, 248 and human colon cell lines, 164

Kola nut, 472 JNK1 KvLQT1, 450 protein kinases, 250 K L86-8275, 199, 207-9 Kaempferol inhibits CYP3A4, 162 Kallikrein and angiotensin converting enzyme (ACE) inhibitors, KCNE1, 450, 451, 452, 453-54 KCNO1, 450, 451, 452, 453-54 Kefauver-Harris Drug Amendments of 1962, 466, 467 Kelch-licke-ECH-associated protein 1 (Keap 1), 246, 247, 251, 252, 253 7-Ketocholesterol and the aryl-hydrocarbon receptor (AhR), 321 Kidney tumors and the EPA, 177 Kinase(s), 212 kinase/phosphatase interactions, 343-45 MAP, 342, 343 protein and the antioxidant response element (ARE), 246-52 rapamycin, 211 serine/threonine kinase antagonists, 207-10 and telomerase, 359-60 tyrosine inhibitors, 200-7 Kinesins and microtubules, 132-33,

134

107

L-778.123, 215-16 L-arginine, 108, 110 and nitrate tolerance, 101 and nitric oxide (NO). 97 L-DOPA and C. elegans, 524 and dopamine transporter (DAT)-KO mice, 264 and Parkinson's disease. L-mevalonate and statins, 108 L-NAME, 107 and penile erections, 113 L-NMMA, 110 Lacidipine, 106 Large intestine cell types in, 159 Large neutral amino acid transporter and the blood-brain barrier, 643-44 Latency associated transcripts (LAT) and HSV-1 infection, 428 LDL See Low-density lipoprotein Lead (Pb) at low doses, 191 Learning, 335, 336 Learning environments, 185 Left ventrical (LV) dysfunction, 107 Legislation for the regulation of drugs and dietary supplements, 467 Lenti vectors and angiotensin converting enzyme (ACE) inhibitors, properties of, 431 Lentiviral vectors

L

and gene therapy, 419-21, 423, 430 nonhuman, 423 Lentivirus(es), 414 and gene therapy, 418, 419-21 Leukemia(s) and Bryo 1, 211 Liver childhood acute lymphoblastic leukemia (ALL), 298 chronic myelogenous leukemia (CML), 200, 202, 219 and R115777, 218 and ras genes, 215 Leukemic cells and edelfosine, 213 Leukotrienes, 84 Life expectancy, 463-64 Life style and drug metabolism, 20, 21 - 22Ligand-binding domain (LBD) and nuclear receptors, 50, 51, 55, 56 Ligands aryl-hydrocarbon receptor (AhR), 309-24 relaxed complex methods to discover, 40-41 Light chemical messengers of, Linear response theory semi-empirical, 39, 41 Lipid(s), 98 and the aryl-hydrocarbon receptor, 319-20 atherogenic, 109-10 lipid A and TLR4 signaling, 621 Lipolysis, 396, 398, 402 Lipopolysaccharide (LPS), 610-22 sensing, 611

sensitivity, 618-21 and survival, 621 set point responses, 618-21 signal transduction, 616-17 signaling complex, 612-13 tolerance, 618 5-Lipoxygenase, 85 and Ad vectors gene therapy, 427 cancer aminoazo dye induced. 3-5.22 and CYP, 149-50 CYP2A6 in, 153 and dose-effect relationships, 499 microsomal enzymes, 8 microsomal monooxygenase, 6-7 microsomes and cytochrome P450. 11, 14 cytochromes in, 9-13 and hydroxylation of testosterone, 9 monooxygenases in, 13-14 tumor(s) and 4-ABP, 499 and aflatoxin B1, 491 induced, 488 and N.N-diethylnitrosamine (DEN), 494-97 Liver-specific transporter-1 (LST), 641 Locally enhanced sampling (LES) method and free energy calculations, 33 Locomotion and dopamine, 526 and dopamine transporter (DAT)-KO mice, 271 in norepinephrine transporter (NET)-KO mice, 274

Locomotor progressive disorder, 534 Long-term depression (LTD), 336 Long-term potentiation (LTP) and NMDA receptors (NMDARs), 335, 336, 344, 345, 347, 349 Long terminal repeats (LTR). 417, 418, 419 and FV vectors, 422 Longevity enhanced, 177 Loperamide and P-glycoprotein, 639 Lovastatin, 572 and Alzheimer's disease. Low-density lipoprotein (LDL) oxidation of, 110 oxidative modification of. and statins, 109 Low-dose linearity, 176 for carcinogens, 177 and hormesis, 192 Low-dose risk assessment and hormesis, 191 Low-dose stimulation, 186 Low-dose stimulatory response and the no observed adverse effect level (NOAEL), 183 Lowest observed adverse effect level (LOAEL). and hormesis, 176 LTB4, 84, 85 Lung cancer and cigarette smoking, and NNK, 498 and polymorphisms, 155-56

240, 242, 243-45, 247,

Magnesium (Mg), 335

and extracorporeal membrane oxygenation

MAHMA/NO. 588

253

Mechanosensation fibrosis, 73-87 (ECMO) therapy, 594, 596 and dopamine, 526 bleomycin (BL) induced, 75-77, 78, 79, 80, 81, Mammalian target of Medical devices 82, 83, 84, 85, 86 rapamycin (mTOR), 211 thrombogenicity of, 593-96 interstitial, 73-87 Mammals injury and lipopolysaccharide Medicine(s) and bleomycin, 75-77, (LPS), 610-11, 615, 618 complementary and and Toll-like receptors alternative medicine non-small cell lung cancer (TLRs), 614 (CAM), 463-82 (NSCLC), 202, 203, 212, Mammary cancer, 5 clinical trials of CAM 214, 217, 218 MAPK therapies, 481 increase in use of, 464 See also Respiratory tract See Mitogen activated LY 294002, 250, 251 protein kinase (MAPK) out-of-pocket Lymphocytes, 609 Market exclusivity expeditures for, 464 Jurkat T. 364 and drugs, 472 product development, Lymphoid Mating 474-75 and dopamine neurons, 526 products, 471 and the immune system, regulation in the U.S., McArdle Laboratory for Cancer Research, 2 466-72 Lymphoma(s), 210 research on, 472-75 mantle cell, 208, 209 McNeil Laboratories, 6 and miltefosine, 213 MD-2, 613, 615, 621 safety of, 466 Melanoma, 210 See also Cancer(s) **MDR** Lys251, 399-400 See Multidrug resistance and Brvo 1, 211 Lysergic acid diethylamide cells, 367 MDR1 C3435T polymorphism of, Melanotransferrin (MTf), 645 (LSD) and dopamine, 525 293-94, 295, 296, 299 Melatonin, 316-17 Lyssaviruses, 422 Melfinavir gene and P-glycoprotein. and the MDRI genotype, M 296 286-89 Ma huang, 472 and SNPs, 289, 292, Melphalan, 643 MAb225 293-94, 297, 299, 300 Memantine murine monclonal and P-glycoprotein, 636 and Alzheimer's disease. structural variability of, antibody, 207 551 Macrophages, 84 289-92 Membrane aspartic protease 2 in chronically inflamed MDR1 mRNA expression, (memapsin2), 553 295 Membrane-associated lung, 77 Lipopolysaccharide (LPS), MDR1 polymorphisms, guanylate kinases 285-301 (MAGUKs) 612, 613 and clinical outcome, Maf proteins and NMDA receptors 297-98 and the antioxidant (NMDARs), 337, 342, response element (ARE), and disease susceptibility, 348, 349

298-300

300-1

and P-glycoprotein

and P-glycoprotein

expression, 294-95,

function, 296-97, 300-1

Memory, 335, 336, 348

546

Meningitis

632

and Alzheimer's disease,

and the blood-brain barrier,

Meningococcal sepsis, 618 2.5-hexanedione transport, 132-34, 135. Meperidine, 6, 7 (2.5-HD), 127 139 and cigarette smoking, 18 3-Methylcholanthrene, 3-5. Sertoli cell(s), 128, 140-41 Meprobamate, 20 7, 9, 10, 11, 12, 22 and the tubulin hypothesis, Mercury and human colon cell lines. 129-32, 139 at low doses, 191 164 Midazolam Metabotropic glutamate (+)-3,4-Methylenedioxand grapefruit juice, 162 receptors (mGluRs), 350 Mild cognitive impairment methamphetamine (MDMA), 273 (MCI), 546 Metachromatic leukodystrophy 06-Methylguanine-DNA-Miller, Drs. James and and gene therapy, 430 methyltransferase Elizabeth, 2 Metal(s) (MGMT), 489-90 Milrinone heavy 4-(Methylnitrosamino)-1and penile erections, 113 and the antioxidant butanone (NNK) Miltefosine, 213 response element and CYPs, 153, 154, 155 Miltex<sup>©</sup>, 213 (ARE), 235, 236 Methylphenidate, 551 Miniature excitatory heavy metal poisoning, 471 and dopamine transporter post-synaptic currents metal ion chelators (mEPSCs), 345-46 (DAT), 267, 526 and dopamine transporter neuroprotective strategy, minK-related protein 1 (DAT)-KO mice, 268-69. (MiRP1), 445 nitric oxide (NO)-releasing 270, 271-72 Minoxidil, 186 metal surfaces, 592, 593 Mibefradil, 16 Mitochondrial dysfunction Metaplasia Mice and DA neuron intestinal, 160, 161 and aflatoxin B1, 491 degeneration, 528 Methamphetamine CYP-knockout, 156 Mitogen activated protein chronic abusers, 277 dopamine transporter kinase (MAPK), 200, and dopamine transporter knockout (DAT-KO) 201, 212, 382, 616 (DAT)-KO mice, 268 mice, 262-72, 273, 275, and adrenergic receptor Methanesulfonanilides, 446. 276-77, 278 polymorphisms (ARPs), 448 lipopolysaccharide 399, 403 Methionine, 215 resistant, 611 pathway Methosymethyl (MOM), 587 transporter mutant, 262-78 lipopolysaccharide 2'-Methoxyacetophenone See also Mouse activated, 613 and CYP2A13, 153 Microsomal epoxide and PD184352, 212 Methyl-β-cyclodextrin, 572 hydrolase (mEH) signaling pathways, 246, 247-50, 252, 253 3-Methyl-4-monomethylamxenobiotic metabolizing, 488, 489 inoazobenzene Mitomycin, 209 (3-Me-MAB), 6, 7, 8 Microsomal metabolism MK-499 and cytochromes P450, and HERG, 446, 448-49 1-Methyl-4-phenyl-1,2,3, 6-tetrahydropyridine 154 Modafinil, 268 (MPTP), 268, 529, 533 Microsomes Molecular dynamics 1-Methyl-4-phenylpyridinium liver, 9-13 simulation(s) Microtubule-associated ion (MPP+), 268, 529, and dynamic pharmacophore models, proteins (MAPs), 130, Methyl n-butyl ketone, 126 132 - 33Methyl n-butyl methane Microtubule(s) of a protein, 31

microtubule-dependent

and relaxed complex

converted to

MRP-efflux systems

and the blood-brain barrier. N methods, 40-41 641 and solvent models, 36-38 Molecular mechanics Multi-unit search for 86 molecular mechanics/ interacting conformers Poisson-Boltzmann-(MUSIC), 40 surface area (MM/PBSA). Multidrug resistance (MDR), 37 - 38286, 635, 638 MOM-PIPERAZI/NO, 587, multidrug resistance 2 589, 591 (MDR2) and P-glycoprotein, 636 Monoamine oxidase (MAO), 263, 267 non-P-glycoprotein and C. elegans, 525 mediated, 641 and dopamine, 528 Multiple sclerosis Monoamine transporters, and the blood-brain barrier, 632 261 - 78Monoclonal antibodies Multivitamins and the Physicians' Health directed against  $A\beta$ , 568-70 Study-II, 111 Monofunctional inducers, Murine leukemia virus 235, 237, 238, 248, (MLV), 419 Murine monoclonal antibody, 253 explained, 234 205-6, 207 Monooxygenases Mutation(s) and cigarette smoking, AFB1-N7-Gua adduct, 492 17 - 18and C. elegans, 522-23, multiple, 8-10, 13-14 530, 531, 532, 534 xenobiotic-metabolizing, 22 and disease, 382 Mood disorders genetic and  $\alpha_{2A}$  adrenergic and Alzheimer's disease, receptor polymorphism 549, 550 (ARP), 400 and hormesis, 183 presenilin missense, 557 Morphine demethylation of, 8 Swedish double, 554 and dopamine transporter and TLR4, 617-18 NAD+ (DAT)-KO mice, 271 MyD88, 614, 616, 621, 622 in norepinephrine Myeloid transporter (NET)-KO and the immune system, 609-10 mice, 274 and P-glycoprotein, Myeloperoxidase 637 - 38and BL-induced lung Mouse fibrosis, 76 Myocardial infarction (MI), C3H/HeJ, 611, 613, 616 smart, 348 104 Naringenin inhibits CYP3A4, 162 and aspirin, 465 See also Mice Moxisylyte, 113 heart failure (HF) after, 107 Nasal mucosa See Respiratory tract

management of, 100

N-acetyl-L-cysteine (NAC), N-demethylase aminoazo dye, 3-4, 6, 10 aminoazo dye N-demethylase and cigarette smoking, 17 N-demethylation, 6, 7 n-hexane, 125-26 converted to 2,5-hexanedione (2,5-HD), 127 polyneuropathy, 126 N-methyl-aniline, 6, 7 N-methyl-D-aspartate (NMDA) and dopamine transporter (DAT)-KO mice, 270 4-(N-methyl-Nnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK), 485, 488, 497-98, 513 N-nitrosodiethylamine (NDEA) and CYPs, 153, 155 N-nitrosomethyl-Namylamine and CYPs, 160 N-nitrosomethylphenylamine and CYP2A13, 153 N'-Nitrosonornicotine, 160 N-nitrosopyrrolidine and PYRRO/NO, 603-4 and BL-induced lung fibrosis, 76-77, 87 NAD(P)H oxidase, 100  $\alpha$ -Naphthoflavone, 13  $\beta$ -Naphthylamine, 2–3 Naproxen sodium and A\(\beta\)42, 563-64

and beta  $(\beta)$ -blockers,

107 - 8

Nasal olfactory tissue and dopamine neuronal and lung fibrosis, 75-76, 84 See Olfactory tissue(s) dysfunction, 521-22 New drug application (NDA), National Advisory Council Neurodegeneration, 521, 522, for Complementary and 527, 529, 530, 531, 532, βNF, 237, 238, 242, 248, 250, Alternative Medicine. 533, 534, 535, 536 473 Neurodegenerative diseases NF-E2 protein, 240, 241, 243, National Center for and scavenger receptors, 244, 245, 246 Complementary and 647 NF-kB, 214, 614, 615, 616, Alternative Medicine Neurological diseases 617 (NCCAM), 463, 471 and gene therapy, 430 N(G)-monomethyl-Land complementary and resistance to xenobiotics. arginine (LNMMA), alternative medicine 157 108 research, 472-75 Neurological disorders Niacin research on St. John's wort and dopamine, 522 and BL-induced lung and other CAM therapies, Neuronal death, 531 fibrosis, 76-77 Neuronal homestasis and ILF, 76-77, 78-79, 84 strategic plan, 473 presynaptic, 262 Nicastrin studies of alternative Neurons and AB, 559 medicine therapies cross-talk between, 346 and y-secretase, 559, 560 interactions with drugs, and dopamine transporter Nicotine 479-80 (DAT)-KO mice, 265 and lung cancer, 156 National Heart, Lung, and Neuroprotective strategies, Nifedipine, 19, 106 552 Blood Institute, 471 and grapefruit juice, 162 National Institutes of Health Neurotoxicity Nisoxetine (NIH), 5, 6, 478 v-diketone, 129 and dopamine transporter and complementary and and 2.5-hexanedione (DAT), 528 alternative medicine (2,5-HD), 126, 129 and dopamine transporter (CAM) research, 472 dopaminergic, 268 (DAT)-KO mice, 269, 270 study on St. John's wort, **MPTP. 268** in norepinephrine 479 in mutant mice, 277 transporter (NET)-KO Native Americans, 464 serotonergic, 268 mice, 275 Natural product(s) Neurotoxins Nitrate(s) and medical practice, dopamine mimetic, 521 ester 464-65 and dopamine transporter nitric oxide regulation in the U.S., (DAT), 526 (NO)-releasing aspirins 466-72 and monoamine as, 103-4 Naveloid transporters, 262 organic, 99-101 and immunity, 622 Neurotransmission tolerance, 100-1 Nebivolol, 107-8 C. elegans, 523 Nitrendipine, 106 Necrosis dopamine, 522, 527, 530 Nitric oxide (NO), 97-114, and Parkinson's disease. Neurotransmitters 106 532-33 and deficits of Alzheimer's and angioplasty, 591 Nervous system disease, 547-48 and angiotensin converting and 2,5-hexanedione and monoamines, 261-62, enzyme (ACE) inhibitors, (2,5-HD), 126, 129, 139 277

Neutrophils

and immunity, 622

C. elegans, 523

Neurobehavioral disorders

bioactivity of, 97-98 and cerebral vasospasm, 598 and CYP3A4 induction. 164 delivery systems, 105 and diazeniumdiolate(s), 585-605 and enzymes, 603 and erections, 601, 603 and ILF, 83-84 inhaled nitric oxide (INO), and mucosal integrity, 102 nitric oxide (NO)-nonsteroidal anti-inflammatory drugs (NSAIDs), 102 nitric oxide (NO)-releasing metal surfaces, 592, 593 and pulmonary hypertension treatment, 600 - 1and statins, 108-9 therapeutic benefits, 604 Nitric oxide synthese(s) (NOS), 84, 97, 110 Nitrite esters, 99-101 Nitroglycerin, 100, 111, 112 Nitrosamine(s) and CYPs, 160 and nasal tumors, 151 Nitrovasodilators, 99-101 NMDA receptors (NMDARs), 335-50 and endoplasmic reticulum retention, 339-41 internalization of, 349-50 and kinase/phosphatase interactions, 343-45 NR2 subunit over-expressed, 348 and plasma membrane.

341, 345

processing in intracellular

compartments, 338-41

and APP y-secretase

proteins that interact with, activity, 574-75 337-38, 350 nitric oxide subunit assembly, 336-37 (NO)-nonsteroidal and the synapse, 335, 336, anti-inflammatory drugs 340, 341, 342-50 (NSAIDs), 102 synaptic and extrasynaptic, Norepinephrine (NE), 403 345-46 and adrenergic receptors N.N-diethylnitrosamine (AR), 381 (DEN), 485, 487, 490, and amphetamine, 267 494-97 and attention-deficit N, N-dimethylaniline hyperactivity disorder and CYP2A13, 153 (ADHD), 271 and C. elegans, 524 NNK See 4-(N-methyl-Nand cocaine responses, nitrosoamino)-1 269 (3-pyridyl)-1-butanone and heart failure, 386, 387 No observed adverse effect norepinephrine transporter level (NOAEL) knockout (NET-KO) concept and derivation of, mice, 273, 274-75, 186, 193 276-78 and hormesis, 175, 176, norepinephrine transporter 177, 187 (NET), 261-62, 268-69, and the hormetic dose response, 179 and psychostimulants, 278 and low-dose stimulatory Nortriptyline, 298 response, 183 and cigarette smoking, 18 Nobel Prize Nose in Physiology or Medicine, and drug delivery, 152 521 See also Olfactory tissue(s) Nobiletin, 13 Nomifensine receptors, 557, 563 and dopamine transporter signaling, 563, 574 (DAT), 528 NR-binding Non-protein sulfhydryl SET-domain-containing (NPSH), 86 protein 1 (NSD1), 57 Non-small cell lung cancer Nrf1, 241, 242, 244, 245 (NSCLC), 202, 203, Nrf3, 245, 246 212, 214, 217, 218 Nrf2 protein Non-steroidal and the antioxidant response element (ARE), anti-inflammatory drugs (NSAIDs) 233, 240-43, 244, 245, 246, 247, 248, 249, 251, and AB42, 563-64 NONOates, 585-605 253 Nonsteroidal Nuclear factor-kB, 78-79, 80, anti-inflammatory drugs (NSAIDs), 102 Nuclear localization signals

(NLS)

and  $\alpha_{2A}$  adrenergic

p and viral vectors, 423 Oncoretroviruses Nuclear receptor corepressor and gene therapy, 418, 419, p23 (N-CoR), 59-60, 62 423 protein, 363 Nucleoside transport systems Oral cavity p120, 58 and the blood-brain barrier. and vinvl acetate in the p300 642-43 drining water, 512 nuclear protein, 54 Nucleotide Oral contraceptives p300/CBP, 54, 55, 61 nucleotide 17, 388 and drug metabolism, 16 p300/Phospho-CREB nucleotide 79, 388 Organ system binding protein (CBP). nucleotide 145, 382 and nitric oxide (NO), 53, 54 nucleotide 901, 400 P448 nucleotide 964, 402 Organic anion transporter cytochrome P448, 11, 12 nucleotide 1165, 383 (OAT), 641-42 P450 nucleotide 1441, 398 Organic anion transporter See Cytochrome P450 polypeptide (oatp), (CYP) 0 641 P/CAF, 53, 54-55, 61, 63 Obesity Orphan Drug Act P-glycoprotein (Pgp) and  $\beta_2$  adrenergic receptor of 1983, 466, 467, 472 and the blood-brain barrier. (AR), 396 Orphenadrine 300, 635-40 and  $\alpha_{2A}$  adrenergic and liver microsomal and disease susceptibility, receptor polymorphism enzymes, 6 298-99 (ARP), 400, 402 OSI-774, 199, 203 and drug-drug interactions, and Arg64 \$3 adrenergic Ovarian cancer cells 288-89 receptor polymorphism, apoptosis of, 367 efflux pump 397-98 Oxaliplatin, 202 at the blood-brain Octopamine Oxidative insult barrier, 635-36 and MDR1 gene, 286-89 and C. elegans, 524 and enzymes, 237 and MDR1 polymorphisms, Office of Dietary Oxidative stress, 233, 246, Supplements., 476 250, 253 291-92, 294-97, 300-1 6-OHDA, 529, 530, 531, 532, and 6-OHDA, 534 physiological role of, 636-37 533, 534, 535 ARE-driven response to, Oil regulation of, 640 **GLA-containing** and cell death, 535 substrates, 286-88, 296-98 and lung disease, 85 and HIV, 297-98 and dopamine neuron Olanzapine (Zyprexa), 551 degeneration, 528 and xenobiotics, 285, 286, Olfactory tissue(s), 512 Oxidized low-density 298 exposure to vinyl acetate, lipoprotein (oxLDL), P13 kinase pathway 508-11 109-10 LPS activated, 613 Oxygen (O) Oltipraz, 238 P13/MAPK, 203 OM99-2 consumption (VO<sub>2</sub>) P waves  $\beta$ -secretase inhibitor, and  $\beta_1$  adrenergic on the ECG, 442 555-56 receptor Paclitaxel, 202, 206, 207 Omeprazole polymorphisms and drug metabolism, 16 (ARPs), 387, 395 and NMDA receptors Oncoretroviral vectors radicals, 98 (NMDARs), 348 and gene therapy, 419 Ozone pollution Panic

and skin cancer, 192

properties of, 431

and liver microsomal receptor polymorphism Peptides (ARP), 400 hormetic effects, 186 enzymes, 6 Phenylethyl isothiocyanate Paracetamol, 513-14 and P-glycoprotein, 637 (PEITC), 244 Paraflex, 6, 7 Pericardium Phenytoin, 296, 638 Parafluorobenzamidine and angioplasty, 591, 592 benzamidine modified into. Perifosine, 213-14 and cigarette smoking, 18 35 Peroxynitrite and drug metabolism, 16 and ILF, 83-84 Phopholipase C, 381 **Parameters** model and nitric oxide (NO), 98 Phosphatidylcholine, 11 Perturbation theory Phosphatidylinositol 3-kinase comparing all, 34-35 Zwanzig's, 32, 35-36 (PI3K), 250-51, 252, Paranoid psychosis PGC-1, 57, 64 and ECG T waves, 443 Phosphodiesterase (PDE), Parkin gene, 535 PGE1, 85 Parkinson, James, 521 PGE2, 85 601 Phosphodiesterase type-5, Parkinsonism pH resistance to xenobiotics. and genetic toxicity, 507 112-13 Phagocytic cells, 609 Phospholipase C, 213 Parkinson's disease (PD), 261 Pharmaceutical industry Phosphorothioate (PS) and cell death, 532-34 and the regulatory PS-DNA oligomers, 365, and dopamine, 521, 522, environment, 466 367 Pharmacist, 1, 2 527, 528-30, 535 Phosphorylation and dopamine transporter **Pharmacokinetics** of adrenergic receptor and the blood-brain barrier, polymorphisms (ARPs), (DAT), 528-30, 535 and gene therapy, 430 629, 630 401, 402 and MRD1 Pharmacophore model(s) and dopamine transporter, dynamic, 39-40 polymorphisms, 300 for mining new drug leads, PKA phosphorylation Paroxetine of Iks, 451, 452 in norepinephrine Phe656, 448 protein, 246, 247, 251-52, transporter (NET)-KO 253 mice, 274 Phenacetin Patent protection and cigarette smoking, 17 Tyr, 210 and drugs, 472 metabolism of, 21 Photooxidation PD 98059, 248, 250, 251 oxidative metabolism of, Trp, 316, 317 Physicians' Health Study-II PDZ proteins and NMDA receptors Phenobarbital, 7, 8, 9, 10, 11, (PHS II) (NMDARs), 335, 337, and antioxidants, 111 340, 341, 342, 343, 348, and drug metabolism, 16, PICK1 349 and dopamine transporter and human colon cell lines. (DAT), 527, 531 Pelle, 621, 622 Pimozide, 525 Pen-2 and liver microsomal PIPERAZI/NO, 588 and  $\gamma$ -secretase, 559, 560 Pirfenidone, 79-80 Pentobarbital, 20 enzymes, 6 and cytochrome P450, Phentolamine P13K/Akt, 211 11 - 12and penile erections, 113 PKA See Protein kinase A Peptide nucleic acids (PNAs) Phenylalanine, 643-44 and telomerase inhibition. Phenylaminopyrimidines, 200 (PKA) 365 Phenylbutazone, 21 Plant biology

and hormesis, 185-86 Polyamine response element cardiac, 443 Plasma membrane (PRE), 246 K+ current and NMDA receptors Polychlorinated biphenyls, 8, delayed rectifier, 445-54 (NMDARs), 341, 345 Pravastatin and proteins, 338 Polyethylenimine (PEI) and Alzheimer's disease. Platelet-activating factor and diazeniumdiolated 573 (PAF), 83, 87 grafts, 594, 595 Pregnenolone-16α-Platelet-derived growth factor Polyglutamine disorders, 534 carbonitrile, 7. (PDGF), 80 Polymorphism(s) 12 platelet-derived growth adrenergic receptor, Prepulse inhibition (PPI), 271 factor (PDGFR) 381-404 Presenilin(s) (PS) and cancer treatments. and C. elegans, 522 and  $\gamma$ -secretase, 557-58, 200, 203, 204 genetic, 165 559, 560-61, 563, 574 Platelets and lung cancer, 155-56 and Alzheimer's disease, MDR1, 285-301 and nitric oxide (NO), 593-96 and clinical outcome. proteins regulating, 559 297-98 and nitric oxide Presynaptic homeostasis (NO)-releasing aspirins, and disease and dopamine transporter 103 susceptibility, 298-300 (DAT)-KO mice, 264-65 Poisons restriction fragment length Prion disease, 534 polymorphism (RELP), ir mune responses to. Pro-prodrug 609 - 22398 and diazeniumdiolates, 604 Poisson-Boltzmann Polyneuropathy and erectile dysfunction, molecular and 2.5-hexanedione 603 mechanics/Poisson-(2.5-HD) exposure, 129 Progesterone, 8 Boltzmann-surface area n-hexane, 126 and St. John's wort, 479 (MM/PBSA), 37-38, 41 Polysaccharides PROLI/NO, 588 Poisson-Boltzmann equation, and diazeniumdiolates, 604 and cerebral vasospasm. 37 Posterior deirids (PDEs) 598, 604 **Pollutants** and C. elegans, 523-24 and erectile response, 603 and the hormetic Postsynaptic density (PSD), Prostaglandin E (PGE), hypothesis, 192 337, 342, 343 84-85 and nasal tumors, 151 PSD-95 Prostaglandin transporter Pollution and NMDA receptors (PGT), 641 and DNA damage, 151 (NMDARs), 337, 342, **Prostaglandins** Poly (ADP-ribose) 343, 344, 345, 347, and the aryl-hydrocarbon polymerase (PAP) 349, 350 receptor (AhR), 319-20 and BL-induced lung Postsynaptic dopamine and aspirin, 465 fibrosis, 76, 77 and mucosal integrity, 102 receptors Poly (vinyl chloride) (PVC) and dopamine transporter Prostate cancer and extracorporeal (DAT)-KO mice, 265-66 and the Physicians' Health membrane oxygenation Potassium (K) Study-II, 111 (ECMO) therapy, 594, and cardiac electrical Protease(s) 596 excitation, 442 caspase 3-like, 213 Polyamine-modulated intramembrane, 557 blockade, 441 factor-1 protein Protein kinase K+ channels (PMF-1), 246 and mammalian dopamine

transporters (DATs), 527 Protein kinase A (PKA) and mammalian dopamine transporters (DATs), 527 PKA phosphorylation of Iks, 451, 452 Protein kinase C (PKC), 209, 210, 211, 320, 640 and ALP analogs, 213 and mammalian dopamine transporters (DATs), 527 and NMDA receptors (NMDARs), 344 signaling pathway, 251-52, 253 Protein phosphatase 1 (PP1), 452 Protein tyrosine kinase (PTK), 345 Protein(s), 381 and  $\beta$ -secretase, 552 and ytsecretase, 559-60 and y-secretase, 574 and 17AAG, 205 adn telomerase, 369 and the antioxidant response element (ARE), 233, 237, 239, 240-46 apoptosis specific protein (ASP), 533 binding and the blood-brain barrier, 630 cap'and'collar (CNC) proteins, 243, 246 cellular retinoic acid binding proteins (CRABPs), 58 CYP. 149-65 cystic fibrosis transmembrane regulator protein (CFTR), 637 decapentaplegic (Smad), 82 diazeniumdiolated and angioplasty, 591-92

and diazenium diolates, 604

in the diet, 18 microtubule-associated and diseases, 534 proteins (MAPs), 130, and dopamine transporter (DAT), 527, 535 and dopamine transporter (DAT)-1, 530, 531, 532 and the endoplasmic reticulum, 338-39 extracellular matrix (ECM) proteins, 73, 75, 77, 78, 82, 85 FKHR, 57 flexibility and computer-aided drug design, 31-41 G-protein(s), 381 coupling, 399 and dopamine transporter (DAT)-KO mice, 265 G-protein coupled receptors (GPCRs), 381, 383, 390, 394 and gene therapy, 413-32 glucocorticoid receptor interacting protein (GRIP1), 55 HERG, 445 hsp90, 310 interactions with, 37 iron transporting, 645 Kelch-licke-ECHassociated protein 1 (Keap 1), 246, 247, 251, 252, 253 kinases pilot studies on, 35 and lipopolysaccharide (LPS), 612, 613, 614, 616-17, 621-22 liver microsomal synthesis, 6 Maf and the antioxidant response element

(ARE), 240, 242,

243-45, 247, 253

132 - 33nitric oxide synthase (NOS), 84 Nrf2 and the antioxidant response element (ARE), 233, 240-43, 244, 245, 246, 247, 248, 249, 251, 253 PDZ. and NMDA receptors (NMDARs), 335, 337, 340, 341, 342, 343, 348, 349 polyamine-modulated factor-1 protein (PMF-1), polypyrimidine tract-binding protein-associated splicing factor (PSF), 62 prenylation, 215 proline-rich nuclear receptor coregulatory proteins (PNRC), 57-58 and proteasome, 214 and reactive nitrogen oxide species (RNOS), 98 receptor interacting protein 140 (RIP140), 60, 61-62, 63, 64 and regulation of antioxidant response element (ARE), 245-46 of retinoic acid receptors (RARs) and retinoid X receptors (RXRs), 51 signaling, 616 and statins, 109 structural fluctuations in. and synaptic transmission, and telomerase, 359-60, 363

telomere binding, 361 transporter (NET)-KO telomeric, 362 mice, 274 that interact with NMDA and serotonin transporter receptors (NMDARs). (SERT)-KO mice, 273 337-38, 350 Public health thyroid hormone receptor agencies interacting protein I and risk assessment/ (TRIPI), 56 thyroid hormone receptor (TR) associate protein 200 (TRAP220), 56 thyroid hormone receptor uncoupling protein (TRUP), 62 and TLRs, 614-15, 616 TRF-1, 362 tyrosine hydroxylase (TH) and dopamine transporter (DAT)-KO mice, 264, 265 See also Amyloid  $\beta$ -protein (A $\beta$ ); P-glycoprotein Proteolysis intramembrane, 556-57 Proteosome, 214 PS1, 558, 559 and Alzheimer's disease. 550, 554-55, 561 OT PS2, 558, 559 and Alzheimer's disease. 550, 554-55, 561 PS-341, 214 Psychiatric disorders and the blood-brain barrier, 632 Psychology experimental and hormesis, 185 **Psychostimulants** and attention-deficit hyperactivity disorder (ADHD), 271

and dopamine transporter

270, 271

in norepinephrine

(DAT)-KO mice, 268-69,

management procedures, 177 and hormesis, 187, 191 Pulmonary hypertension and diazeniumdiolates. 600 - 1Pure Food and Drugs Act of 1906, 466, 467 Pyrazole and human colon cell lines. 164 Pyridine, 17 PYRRO/NO, 588, 589, 603 and hepatocarcinogens. 603 - 4Pyrrolidinedithiocarbamate (PDTC), 244 Q ORS complex on the ECG, 442-43 acquired long QT syndrome, 443 dynamics and sildenafil citrate, 112 interval on the ECG, 442, 443 prolongation of, 441, 443, 449, 453, 454 long OT syndrome congenital, 449 prolongation, 453 and drugs, 444 Ouercetin inhibits CYP3A4, 162 Quetiapine (Seroquel), 551 Quinidine, 288, 444, 448

and drug metabolism.

15 - 16

**Ouinones** and DA, 528

R R115777, 217-18 Raclopride, 270 RAD001, 212

and dopamine transporter (DAT)-KO mice, 271 Radiation, 73, 209 and germ cell apoptosis, 136 and the hormetic hypothesis, 192 interest in low-dose stimulation, 192 risk extrapolation model of. 486

Ralitrexed, 202 Rapamune, 199, 211-12 Rapamycin, 199, 211-12 mammalian target of rapamycin (mTOR), 211 Reactive nitrogen oxide species (RNOS), 97-98

Reactive oxygen species (ROS), 76, 79, 80, 81, 84, 85, 184 and dopamine, 528, 529,

Receptor-associated cofactor 3 (RAC3), 55

Receptor interacting protein 140 (RIP140), 60, 61-62, 63, 64

Receptor mediated transport (RMT), 629, 631, 634, 635, 644-45

Receptor-mediated transport (RMT), 631

Receptor(s) adrenergic, 381-404 flexibility and protein-ligand interactions, 31

NMDA, 335-50

cytochrome P450 in, 150,

151-58, 164

Restenosis

scavenger after angioplasty, 585, properties of, 431 590-93 and the blood-brain Retroviruses barrier, 646-47 and nitric oxide (NO) structure and replication, Toll-like receptors (TLRs), delivery systems, 105 417-19 609-22 reducing, 104 and transduction, 422-24 Reductase Restriction fragment length Rhabdovirus family, 422 azo-link, 3-4 polymorphism (RELP), Rheumatoid arthritis, 73, 85 398 Regulatory agencies and risk assessment, 176 Retinaldehyde, 47 and statins, 108, 109 and risk assessment/ Retinoic acid (RA) Ribozymes active ingredient of vitamin management procedures. and telomerase, 363, 367 177 A, 47-48 Rifampicin Regulatory statutes and the aryl-hydrocarbon and drug metabolism, 16 Federal, 466-67 receptor (AhR), 320 Rifampin, 287, 288, 289 Relaxed complex methods nuclear receptors for, Risk to discover ligands, 40-41 48-49 assessment, 175 Remediation technology, 192 retinoic acid response cancer and noncancer Renal epithelial tumor elements (RAREs), 49, harmonization of. and MDRI 175, 189-91 51,52 polymorphisms, 299 Retinoic acid receptors carcinogen, 188-89, 486 (RARs), 47 governmental procedure, renin-angiotensinand the aryl-hydrocarbon 177 receptor (AhR), 320, 321 and hormesis, 184, aldosterone pathway, 107 coactivators of, 53-59 186-92 coregulators of, 47, 51-64 non-cancer, 193 Repolarization cardiac, 451, 453-54 corepressors of, 59-62 non-carcinogen, 188 domain features of, 49-50 and HERG channels. pardigms, 176 445 and the retinoic acid (RA) communication and IKs, 450 receptor family, 48-49 and hormesis, 191-92 and cardiac electrical Retinoid X receptors (RXRs), evaluation excitation, 442 AFB1, 494 cellular, 441, 450, coactivators of, 53-59 carcinogenic, 486 453-54 coregulators of, 47, 51-64 Risperidone (Risperdal), 551 Ritonavir, 297, 639 disruption of, 449 corepressors of, 59-62 ventricular, 449 domain features, 49-50 Rivastigmine (Exelon) Reservine and the retinoic acid (RA) and Alzheimer's disease, and CYP3A5, 164 receptor family, 48, 49 551 Respiratory difficulties Retinoid(s) RNA and Alzheimer's disease, and the aryl-hydrocarbon hTR RNA template, 359, 363, 365, 367 546 receptor (AhR), 320-21 and lentiviral vectors, 420, Respiratory tissue receptors, 47-64 and vinyl acetate exposure, Retroviral vector(s) 424 mRNA and adenoviral 511-12 in clinical trials, 429-30 Respiratory tract development and vectors, 424

production, 419-22

and gene therapy, 414,

417-24

and retroviral vectors.

417-19, 420, 421

and telomerase, 360

hyperactivity disorder

RO-32-0432, 251 Rohitukine, 207 Rotenone, 529 and cell death, 533 Rusch, Dr. Harold, 2 RXT ER retention motif, 338-39, 340

#### S

S-nitroso-albumin, 101 S-nitroso-captopril, 102 S-nitroso-diclofenac, 105 S-nitroso-glutathione, 101 S-nitroso-Nacetylpenicillamine, 101 S-nitroso-nonsteroidal anti-inflammatory drugs (NSAIDs), 105 S-nitrosothiols and nitric oxide (NO), 101 - 2Salicin, 465 Saguinavir, 297 and grapefruit juice, 163 Sarcomas, 202 Saroidosis, 73 SB202190, 249 SB203580, 249, 250, 251 Scavenger receptors and the blood-brain barrier, 646-47 SCH23390, 270 and dopamine transporter (DAT)-KO mice, 271 SCH66336, 217 Schizophrenia, 261, 336 and adrenergic receptor polymorphisms (ARPs), 399, 400 and dopamine, 270, 522 Sclerosis systemic, 73 α-Secretase enhancement of activity of,

571-72

B-Secretase, 571

cell biology of, 554 explained, 548 inhibition of, 552-56, 573 protease biochemistry of, 552-53 strategies to identify inhibitors of, 555-56 substrate specificity of, 554-55 v-Secretase, 550, 574 explained, 548 inhibition of, 556-64, 573 inhibitors and AB, 561-64 as a multi-protein complex, 559-60 and nonsteroidal anti-inflammatory drugs (NSAIDs), 574-75 and presenilin, 557-58, 559, 560-61, 574 Seizures and the blood-brain barrier. 632 Selegiline 552

and Alzheimer's disease, 552 Self-inactivating vectors (SIN), 419 and lentiviral vectors, 420 Selye, Hans, 7 Senescence cell, 373 at the telomeres, 362 Sensitivity analysis systemic, 34–35, 41 Sensory experience

receptors (NMDARs), 346 Ser 49, 382, 383, 384–85 Serine, 215 serine/threonine kinase

and synaptic NMDA

antagonists, 207–10 Serotonin, 276, 277, 316–17 and amphetamine, 267 and attention-deficit

(ADHD), 271 and C. elegans, 523, 524 and cocaine responses, 269 and dopamine transporter (DAT)-KO mice, 270 and dopaminergic hyperactivity, 270 and locomotion, 272 and psychostimulants, 278 serotonin transporter knockout (SERT-KO) mice, 272-74, 275, 276-77, 278 serotonin transporters (SERT), 261, 262, 268, 269 Sertoli cell(s), 128-29

and 2,5-hexanedione (2,5-HD), 126, 136 and cytoplasmic dyneins, 133 ectoplasmic specializations, 135 and germ cells, 135 and kinesin, 133 microtubule-dependent transport, 139 microtubules, 140-41 and SCF, 137 and testicular atrophy, 131 Sertraline

Sertraline and St. John's wort, 479 Serum amyloid-P (SAP), 564–65

Severe combined immunodeficiency-X1 (SCID-X1) and gene therapy, 429 Shock 612

Shock, 612
agent responsible for, 610
Signal transduction
and the aryl-hydrocarbon
receptor (AhR), 309–11
and cancer treatments.

199-220

Na+ channels, 448

and cardiac electrical

excitation, 442, 443

and the endotoxin receptor, Sodium nitroprusside (SNP) hydroxylation of, 12 and nitric oxide (NO), 99 metabolism of, 9-10 616-17 and tyrosine kinase, 613 Solvent models and microsomal enzymes, Signaling pathways and free energy and the antioxidant calculations, 32, 36-38, steroid receptor coactivator response element (ARE). (SRC), 53, 54, 55 246-52, 253 Sotalol (Betapace), 444, 447 STI-571 Sildenafil (Viagra), 112-13, SPACE trial, 111 and cancer treatment, 199. 444, 601, 603 SPER/NO 200, 202, 219 Silencing mediator for and angioplasty, 591 Stilbene, 453 retinoid and Spermatogenesis, 129, 133 Stomach thyroid-hormone and apoptosis, 134 cancer, 160-61 receptors (SMRT), and GnRH agonist, 138 cell types in, 159 59-60, 62 and Sertoli cells, 141 cytochrome P450 in, 151, and the Steele-Dickie Simian immunodeficiency 160-61virus (SIV), 423 mouse, 137-38 Streptavidin Spermine, 587, 588, 591 and binding affinities, 37 Simulation methods and drug design, 31-32 Spermtogenesis, 137 Stress Simvastatin, 109, 572 and Sertoli cell and HSV-1 infection, 428 Single nucleotide microtubules, 140 and learning performance, polymorphisms (SNPs), Spinocerebellar Ataxias, 534 Spumaviruses Stroke 108, 382, 386, 390, 392, 393, 394-95, 398, 399 and aspirin, 465 and gene therapy, 418 drawbacks of, 101 St. John's wort, 288, 479, 482 and cerebral vasospasm, intravenous, 100 and depression, 481 and MDR1 gene, 289, 292, and drug metabolism, 16 and nitric oxide (NO), 98 293-94, 297, 299, 300 Statins, 108-9 Structure/function claims and penile erections, 113 and Alzheimer's disease, and dietary supplements, Sirolimus, 199, 211-12 573 468 Skin cancer StatV Styrene oxide, 488, 489 and ozone pollution, 192 B-secretase inhibitor, SU0020, 204 Small intestine 555-56 SU101, 203-4 SU5416, 204 cell types in, 159 Staurosporine, 251 cytochrome P450 in, 151, 7-OH, 199, 209-10 Substantia nigra 161-63 Stem cell factor (SCF), of MPTP-treated dopamine Small unique nuclear receptor 136 - 38transporter (DAT)-KO corepressor (SUN-CoR), Stem cell gene therapy, 430 mice. 268 and Parkinson's disease, Smokers, 19 in balloon angioplasty, 590 529 and nasal tumors, 151 nitric oxide Substantia nigra pars See also Cigarette(s) (NO)-releasing, 592 compacta (SNpc) Smoking Steroid(s) dopamine neuronal death, See Cigarette(s); Smokers and the aryl-hydrocarbon 529 Sodium (Na) receptor (AhR), 319-20 and Parkinson's disease.

hormones

17

and cigarette smoking,

528

Subunit assembly

in the endoplasmic

and free energy

calculations, 32-33

reticulum, 338-39 on the ECG, 442, 443, 449, (2.5-HD), 125-41 and NMDA receptors 454 toxicant-induced, 139 (NMDARs), 336-37 TAB1, 616 Testosterone SUGL 56 TAB2, 616 hydroxylation of, 8-10, Sulfhydryl group(s) **Tachyarrhythmias** and the antioxidant supraventricular, 443 and testicular atrophy, 138, response element (ARE), Tachyphylaxis, 393-94 139 Tacrolimus, 294 2,3,7,8-Tetrachlorodibenzo-235, 246, 252 Sulforophane (Sul), 248 and diltiazem, 639 p-dioxin (TCDD) Sulfur amino acid deprivation TAK1, 616 and the arvl-hydrocarbon Tangeretin, 13 (SAAD), 250 receptor (AhR), 309, 310, Tarceva<sup>TM</sup>, 199, 203 Sulindac sulfate 311, 313, 316, 317-18, Taurine, 77, 78, 79, 84 and AB42, 563-64 319-20, 321 Superoxide ion Taxol, 209 and CYPs, 154, 156-57 and Parkinson's disease. and spermtogenesis, 140 and human colon cell lines, 529 Taylor's series expansion, Superoxide radical, 100 34-35 Tetraethyl ammonium (TEA), and dopamine, 528 Teas 448 Tetrahydroaminoacridine and nitric oxide (NO), 98 and aryl-hydrocarbon Survival receptor (AhR) ligands, (Cognex) and Alzheimer's disease, and lipopolysaccharide 313 (LPS) sensitivity, 621 Telomerase, 359-74, 373 SWI/SNF genes, 56 inhibition of, 360, Tetrahydrobenzodiazepine. Sympathetic nervous system 363-73 216 stimulation Telomere(s) Tetrahydrobiopterin and sudden cardiac death. and nitrate tolerance, 101 capping, 362 453 inhibition and disruption. Tetrapeptide, 215 Synapse 359-74 Tetrapyroles structure and function of. and NMDA receptors and the aryl-hydrocarbon (NMDARs), 335, 336, 360-62 receptor (AhR), 318-19 340, 341, 342-50 targeting of, 368-73 Thalidomide silent synapse hypothesis, Temozolamide, 210 crisis of 1962, 466 Terbutaline, 395, 396 Theophylline and cigarette smoking, 18 Syntaxin Terfenadine (Seldane), 443, and dopamine transporter 444, 447, 448 oxidative metabolism of. (DAT)-1, 530-31 and grapefruit juice, 163 18 α-Synuclein, 527, 531, 534, Therapeutic agents tert-butylhydroquinone (tBHQ), 236, 237, 238, 535 and CYPs, 150 239, 240, 242, 244, 248, and nasal tumors, 151 Systematic sensitivity **Therapeutics** analysis 250, 251 systematic, 34-35, 41 Testicular atrophy, 126, complementary and 129 alternative, 463-82 Systole, 442 persistance of, 137, 138 Thermodynamic T and Sertoli cells, 131 cycle-perturbation therapy for, 138-39 T cells method

Testicular injury

and 2,5-hexanedione

and gene therapy, 429, 430

T wave

Thin-layer chromatography (TLC) and C. elegans, 524 Thiocyanate toxicity, 99 Thiols and nitrate esters, 100 and nitrate tolerance, 101 Thioredoxin, 253 Thioridazine (Mellaril), 443, 444 Thr164, 388, 389, 390, 395 Thr623, 448 Threonine, 212 serine/threonine kinase antagonists, 207-10 Threshold mechanisms and carcinogens, 487-91 Thrombin, 103 Thrombogenicity of medical devices, 593-96 Thrombosis, 108 and nitric oxide (NO) delivery systems, 105 therapy for, 102 Thromboxane and NCX-4016, 104 Thyroid hormone receptor associate protein 200 (TRAP220), 56 Thyroid hormone receptor interacting protein I (TRIPI), 56 Thyroid hormone receptor uncoupling protein (TRUP), 62 Thyroid response element (TRE), 59 Tissue factor (TF) and NCX-4016, 104 Tissue plasminogen activator (tPA), 204 Tissues extrahepatic, 165 and CYPs, 150, 157

Tobacco smoke

environmental, 498

and nasal CYPs, 157

See also Cigarette(s) Toll/IL-1 receptor/resistance (TIR domain), 614-15. 616 Toll-like receptor(s) (TLR), 609-22 evolution of, 614-15 structure, 615-16 TLR1, 622 TLR2, 613, 615, 616, 617 TLR3, 613, 615 TLR4, 613, 616, 617 and changes in chromatin structure, and lipopolysaccharide (LPS), 614, 615 mutations at, 617-18 signaling pharmacological blockade of, 621-22 TLR5, 613 TLR6, 622 TLR7, 622 TLR8, 622 TLR9, 613, 617 TLR10, 622 Topotecan, 202 Tourette syndrome, 261 Toxic substances at low doses, 191 low doses of, 177 Toxicant(s) and CYPs, 150 exposure and germ cell apoptosis, risk assessment of, 150, 151 Toxicity chemical, 165 and CYPs, 150 developmental, 154 and diazeniumdiolates. 603-4 y-diketone-induced, 126

of nonsteroidal

anti-inflammatory drugs (NSAIDs), 102 respiratory, 156 single nucleotide polymorphisms (SNP), 99 systemic and lung fibrosis treatment, 74, 80, 84, xenobiotic, 152, 156 Toxicological literature hormesis in, 179 Toxicological studies and hormesis, 177 Toxicology community and hormesis, 176-77 definition of, 175 definition should be changed, 176 and the dose-response revolution, 176-77 and hormesis, 175, 193 **Toxins** environmental, 535 immune response to, 609-22 TPA, 251 TPA-response element (TRE) and the antioxidant response element (ARE), 239, 240, 242 Trachea See Respiratory tract TRAF6, 616 Trans Golgi network (TGN) and NMDA receptors (NMDARs), 341 Transcription and the antioxidant response element (ARE), 233, 235, 236, 237, 240-46, 247, 248, 249, 250, 251-52, 253 Transcritional intermediary factor I (TIFI), 55

Transduction	Tubulin, 140	and DNA adducts, 498
adeno-associated viral	and testicular injury,	and DNA repair
(AAV) vector, 416-17	129–32, 139	enzymes, 490
and adenoviral vectors,	Tumor necrosis factor (TNF),	nasal, 151
426-27	204	and rapamycin, 211
and HSV-1 vector, 428-29	and endotoxicity, 612	rates
and retroviruses, 422-25, 430	and lipopolysaccharide (LPS), 617	and apoptosis, 491 and signal transduction
Transferrin-receptor 1	mRNA translation, 616	inhibitors, 219
(Tf-R1), 644	and TLR4, 615	and STI-571, 202
Transferrin-receptor 2	and TLRs, 617	and trastuzumab, 205–7
(Tf-R2), 644–45	TNF-α, 79, 80, 83	and UCN-01
Transforming growth	apoptosis induced by,	and vinyl acetate exposure,
factor- $\beta$ , 77–82, 83, 85,	104	504–5
87	and Bryo 1, 211	and ZD 1839, 202
Transport systems	and NCX-4016, 104	Twins
nucleoside	Tumorigenesis	and drug metabolism, 20
and the blood-brain	and CYPs, 154	Type II cells, 151–52
barrier, 642-43	Tumor(s)	Tyr652, 448
Transporter(s)	and 17AAG, 205	Tyrosine, 212
anion influx and efflux	and CCI-779, 212	and NMDA receptor
and the blood-brain	cell population doublings,	(NMDAR)
barrier, 641-42	362	internalization, 349, 350
and the blood-brain barrier,	cells	Tyrosine hydroxylase (TH)
631	and edelfosine, 213	and C. elegans, 524
large neutral amino acid	and MAPK, 212	and dopamine transporter
and the blood-brain	and PS-341, 214	(DAT)-KO mice, 264,
barrier, 643-44	and SCH66336, 217	526-27
Trastuzumab, 206-7	and cetuximab, 207	inhibition, 266
Trauma, 73	and farnesly transferase	Tyrosine kinase
Trichloroethylene	inhibitors, 215	Ber-Abl, 200
and carcinogenesis, 486,	and flavopiridol, 208-9	c-Kit, 136-37
488	formation	inhibitors, 200-7
Troleandomycin, 160	and hormesis, 183-84	in lipopolysaccharide
Trypsin, 35	and vinyl acetate, 512	(LPS) signaling, 613
Tryptamine	vinyl acetate exposure,	
and the aryl-hydrocarbon	511	U
receptor (AhR), 317, 321	growth	U0126
Tryptophan (Trp)	and anti-cancer agents,	UCN-01, 199, 209-10
and the aryl-hydrocarbon	192	UDPGT*01
receptor (AhR), 314, 321	inhibition of, 200	and the aryl-hydrocarbon
and aryl-hydrocarbon	low-dose enhancing, 186	receptor (AhR), 318
receptor (AhR) ligands,	and hormetic dose	UGT*01
316–17	response, 193	and the aryl-hydrocarbon
and dopamine transporter	incidence	receptor (AhR), 318
(DAT) KO mice 270	and call avala arrest	Illoggo

and cell cycle arrest,

490

Ulcers

and gastrointestinal

(DAT)-KO mice, 270

Trp64, 396, 397

98

and cancer risk, 238 toxicity, 102 University of diet. 19 Veins Wisconsin-Madison Allan H. Conney at, 2 and beta  $(\beta)$ -blockers, Urinary tract infection (UTI), 107 - 8Venodilation 476 U.S. Environmental and beta  $(\beta)$ -blockers. Protection Agency 107-8 (EPA), 177 Ventricle(s) and cardiac electrical U.S. Federal Drug Administration (FDA), excitation, 441-42 left ventricle (LV) 177 **UV** irradiation and intravenous and HSV-1 infection. nitroglycerin, 100 428 Verapamil, 639 and grapefruit juice, 163 V Vesicles V-PYRRO/NO and NMDA receptors heptatoprotective, 603 (NMDARs), 341 Vaccines, 466 Vesicular monoamine reduced the number of deaths, 464 Val625, 448 Valsartan, 107 Vardenafil and penile erections, 113 Vascular disease and chelation therapy, 471 Vascular endothelial growth factor (VEGF), 204 Vascular grafts and diazeniumdiolates, 593-94, 595 Vasodilation and AT-1 antagonist, 107 and calcium channel

transporter 2 (VMAT2) and C. elegans, 524 Vesicular monoamine transporters (VMATs) and C. elegans, 524 Viagra, 444 Vinblastine, 638-39 Vinvl acetate carcinogenicity studies with inhalation exposure, carcinogenicity studies with oral exposure, 501-5 epidemiological studies of carcinogenicity of, 506-7 as a genotoxic carcinogen, 485, 486, 499-513 blockers (CCBs), 106 and nebivolol, 108 inhalation exposure to, 508 metabolism and and nitric oxide (NO), genotoxicity of, 507-8 Vasorelaxation occupational exposures to, and nitrates, 99 513 Vasospasm, 596, 598-99 oral exposure to, 501-5 Vegetable(s) practical threshold for and aryl-hydrocarbon carcinogenesis, 508-13 receptor (AhR) ligands, Viral infections, 22 313 Viral vectors

in clinical trials, 429-30 gene therapy with, 413-32 integrating and nonintegrating, 414 Virus(es) and gene therapy, 413-32 helper, 414-15 Visna, 423 Vitamin A and retinoic acid (RA), 47-48, 49 Vitamin C. and Alzheimer's disease, 552 and LDL oxidation, 110 and the Physicians' Health Study-II, 111 and S-nitrosothiols, 101 Vitamin D receptor (VDR), 56 Vitamin E and Alzheimer's disease, and cardiovascular events. and the Physicians' Health Study-II, 111 VMAT2, 264, 267, 277 W Watercress, 19 West Nile fever, 464 Willow tree therapeutic benefits of, 464 Wine and cardiovascular disease. Withering, William, 466 Wood dust

X XE991, 453 Xenobiotic(s) compounds

Wortmannin, 250

and nasal tumors, 151

and CYPs, 150
and cytochrome P450
enzymes, 149–50
and the respiratory tract, 151
enzyme induction by, 234, 235–38
metabolic activation of, 152
metabolism, 7, 8, 13–22
and CYPs, 149–65
G.I. tract, 158–59

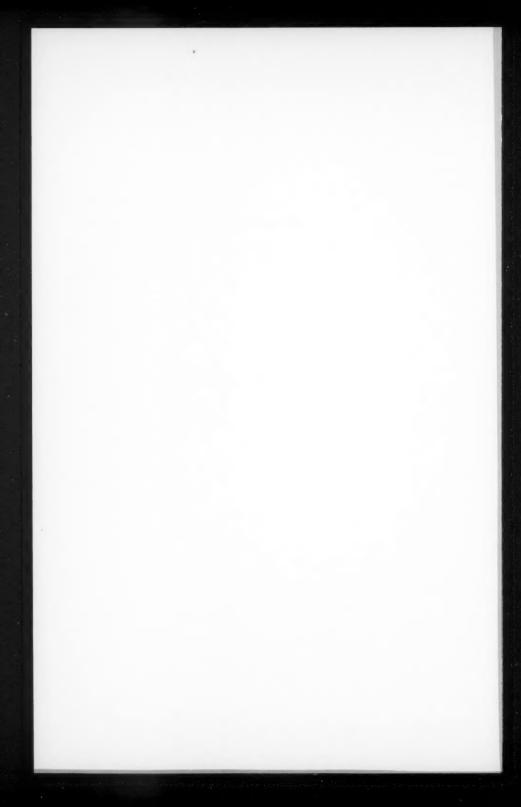
and hydrocarbons,

17-18

metabolizing enzymes
and aryl-hydrocarbon
receptor (AhR) ligands,
309, 310, 323
neurotoxic, 300
and P-glycoprotein, 285,
286, 298
and the smalll intestine,
161
study of the adverse effects
of, 175
xenobiotic response
element (XRE), 234, 235,
238, 250

Y
Yerkes, Robert, 185
Yerkes-Dadson Law, 185
Yohimbine, 113

Z
ZD 1839
and cancer treatment, 199, 202–3
Zoxazolamine, 6, 7, 13
hydroxylase
and cigarette smoking, 17
hydroxylation of, 14–15



## **CUMULATIVE INDEXES**

## **CONTRIBUTING AUTHORS, VOLUMES 39–43**

#### A

Adams JP, 42:135-63 Allen JW, 39:151-73 Allio T. 43:125-47 Altman RB, 42:113-33 Amara SG, 39:431-56 Ambudkar SV, 39:361-97 Anderson SP, 40:491-518 Angers S, 42:409-35 Aschner M, 39:151-73 Atkinson AJ Jr, 41:347-66

#### R

Bagdassarian CK, 41:661-90 Baker RC, 39:127-50 Balboa MA, 39:175-89 Baldwin LA, 43:175-97 Balsinde J, 39:175-89 Barber DL, 42:527-52 Barnes PJ, 42:81-98 Bearss DJ, 43:359-79 Bertaccini E. 41:23-51 Beutler B, 43:609-28 Blackburn TP, 40:319-34 Blau HM, 40:295-317 Bode-Böger SM, 41:79-99 Böger RH, 41:79-99 Blakely RD, 43:521-44 Boekelheide K, 43:125-47 Bogdanffy MS, 43:485-520 Bolt HM, 43:485-520 Borges K, 39:221-41 Borjigin J, 39:53-65 Bortner CD, 42:259-81 Bouvier M, 42:409-35 Bradfield CA, 40:519-61 Branchek TA, 40:319-34 Breyer MD, 41:661–90

Breyer RM, 41:661-90 Broder S, 40:97-132 Brown JH, 40:459-89 Brunton LL, 41:751-73 Burgen ASV, 40:1-16 Burke MD, 41:297-316

C Calabrese EJ, 43:175-97 Carlsson A, 41:237-60 Carlsson ML, 41:237-60 Chan PLS, 41:625-59 Changeux J-P, 40:431-58 Choudhuri S, 39:267-94 Caron MG, 43:261-84 Chun J, 41:507-34 Cidlowski JA, 42:259-81 Clancy CE, 43:441-61 Coles P. 41:175-202 Collins MD, 39:399-430 Conney AH, 43:1-30 Contos JJA, 41:507-34 Corringer P-J, 40:431-58 Corton JC, 40:491-518 Coyle JT, 42:165-79

#### D

Dalton TP. 39:67-101 Davis KL, 41:203-36 Debouck C, 40:193-208 de Boer AG, 43:629-56 Defer N. 41:145-74 de Groat WC, 41:691-721 Denhardt DT, 41:723-49 Denison MS, 43:309-34 Denker SP, 42:527-52 Dennis EA, 39:175-89 De Vries L, 40:235-71 Dey S, 39:361-97

Ding X, 43:149-73 Dingledine R, 39:221-41 Doull J. 41:1-21 DuBois RN, 42:55-80

# E

Eichelbaum M, 43:285-307 Elenko E. 40:235-71 Elliott JD, 40:177-91 Elsayed Y, 43:199-231 Embree-Ku ME, 43:125-47 Eudy JD, 42:181-208 Evans WE, 41:101-21

#### E

Farquhar MG, 40:235-71 Fernandez EJ, 42:469-99 Finnell RH, 42:181-208 Fischer T, 40:235-71 Fleming SL, 43:125-47 Flexner C, 40:651-76 Fromm MF. 43:285-307 Fu H. 40:619-49 Fukushima N, 41:507-34

#### G

Gaillard PJ, 43:629-56 Gainetdinov RR, 43:261-84 Gelineau-van Waes J. 42:181-208 Giachelli CM, 41:723-49 Gillette JR, 40:19-41 Giri SN, 43:73-95 Golding BT, 42:325-48 Goodman JI, 42:501-25 Goodwin B, 42:1-23 Gottesman MM, 39:361-97 Greenlee WF, 41:297-316 Griffin RJ, 42:325-48

Gu Y-Z, 40:519–61 Guengerich FP, 39:1–17 Guyton KZ, 41:421–42

#### H

Hall SJ, 43:125-47

Hammond HK, 39:343-60 Hanoune J, 41:145-74 Hardcastle IR, 42:325-48 Harris RA, 41:23-51 Hengstler JG, 43:485-520 Hickson ID, 41:367-401 Hobbs AJ, 39:191-220 Hogenesch JB, 40:519-61 Hogg N, 42:585-600 Holford NHG, 40:209-34; 41:625-59 Holm-Waters S, 41:237-60 Hook SS, 41:471-505 Houghten RA, 40:273-82 Hrycyna CA, 39:361-97 Hurley LH, 43:359-79

#### 1

Ignarro LJ, 43:97–123 Insel PA, 39:175–89, 343–60; 41:593–624 Ishii I, 41:507–34

#### J

Javitch JA, 42:437–67 Johnson DG, 39:295–312 Johnson KJ, 43:125–47 Juliano RL, 42:283–323

#### K

Kaminsky LS, 43:149–73 Kass RS, 43:441–61 Kedzierski RM, 41:851–76 Keefer LK, 43:585–607 Kenakin T, 42:349–79 Kensler TW, 41:421–42 Kim G, 43:199–231 Kim RB, 41:815–50 Kimelberg HK, 39:151–73 Kimko HC, 40:209–34 Kinsel JF, 43:463–84 Kitteringham NR, 41:443–70 Klaassen CD, 39:267–94 Klein PS, 41:789–813 Klein TE, 42:113–33 Kliewer SA, 42:1–23 Kootstra NA, 43:413–39 Kramer RE, 39:127–50 Kurokawa J, 43:441–61 Kwon EJ, 43:125–47

#### L

Law P-Y, 40:389-430 Lebedeva I. 41:403-19 Lee HC, 41:317-45 Lee SJ, 41:569-91 Lefer DJ, 40:283-94 Le Novère N, 40:431-58 Lesko LJ, 41:347-66 Li T-K, 41:53-77 Li X. 39:53-65 Liggett SB, 43:381-411 Lin JH, 41:535-67 Linden J. 41:775-87 Liu J, 39:267-94 Liu LF, 41:53-77 Loh HH, 40:389-430 Lolis E. 42:469-99 LoPachin RM, 39:151-73 Lu AYH, 41:535-67

#### M

Maliakal P, 42:25–54 Mao GE, 39:399–430 Marnett LJ, 42:55–80 Martin E, 41:203–36 Masters SC, 40:619–49 McCammon AJ, 43:31–45 McEwen BS, 41:569–91 McGraw DW, 43:381–411 McLeod HL, 41:101–21 Means AR, 41:471–505 Melvin WT, 41:297–316 Meng X, 42:25–54 Metcalf B, 40:193–208 Michel JJ, 42:235–57 Moncada S, 39:191–220 Monga M, 43:199–231 Monteleone JPR, 40:209–34 Montfort WR, 41:261–95 Murad F, 41:203–36 Murray GI, 41:297–316 Myers SA, 41:661–90 Myers SJ, 39:221–41

#### P

Nagata K, 40:159–76 Nagy SR, 43:309–34 Napoli C, 43:97–123 Nass R, 43:521–44 Negishi M, 41:123–43 Nemeroff CB, 41:877–906 Neu J, 42:381–408 Nguyen T, 43:233–60 Nilsson M, 41:237–60 Norbury CJ, 41:367–401 North RA, 40:563–80

#### 0

Oesch F, 43:485–520 Ohlstein EH, 40:177–91 O'Neill PM, 41:443–70 Otterness DM, 39:19–52 Owens MJ, 41:877–906 Ozawa CR, 40:295–317

#### P

Park BK, 41:443–70 Pastan I, 39:361–97 Patel SR, 43:125–47 Peck CC, 40:209–34 Petralia RS, 43:335–58 Phiel CJ, 41:789–813 Pickett CB, 43:233–60 Plaa GL, 40:43–65 Pootoolal J, 42:381–408 Posner GH, 41:421–42 Post SR, 39:343–60 Powis G, 41:261–95 Puga A, 39:67–101 Prybylowski K, 43:335–58 Putney LK, 42:527–52

#### R

Ramachandra M, 39:361–97 Ramos KS, 39:243–65 Rana BK, 41:593–624 Rasoulpour RJ, 43:125–47 Redinbo MR, 42:1–23 Rezler EM, 43:359–79 Rittling SR, 41:723–49 Rosenquist TH, 42:181–208 Ruffolo RR Jr, 40:177–91

#### S

Sagi SA, 40:459-89 Sah VP, 40:459-89 Salahpour A, 42:409-35 Sans N. 43:335-58 Sausville EA, 43:199-231 Schenk D. 43:545-84 Schoenfeld HA, 43:125-47 Schwab M. 43:285-307 Scott JD, 42:235-57 Seal RP, 39:431-56 Seasholtz TM, 40:459-89 Selkoe DJ, 43:545-84 Sheiner L, 40:67-96 Sherratt PJ, 43:233-60 Shertzer HG, 39:67-101 Shi L. 42:437-67 Shiina T, 41:593-624 Shoham M. 41:175-202 Sibley DR, 39:313-41 Small KM, 43:381-411 Snyder SH, 39:53-65 Springer ML, 40:295-317 Standley S, 43:335-58

Starkov AA, 40:353-88 Stauber A. 40:491-518 Steimer J-L, 40:67-96 Stein CA, 41:403-19 Stein CM, 41:815-50 Steinberg SF, 41:751-73 Stout SC, 41:877-906 Strassburg CP, 40:581-618 Streit WJ, 39:151-73 Straus SE, 43:463-84 Subramanian RR, 40:619-49 Sueyoshi T, 41:123-43 Surprenant A, 40:563-80 Svensson CI, 42:553-83 Sweatt JD, 42:135-63 Szumlanski CL, 39:19-52

#### T

Tateyama M, 43:441–61 Taylor SL, 42:99–112 Tedroff J, 41:237–60 Thibonnier A, 41:175–202 Thibonnier M, 41:175–202 Thompson S, 43:125–47 Trudell JR, 41:23–51 Tsai G, 42:165–79 Tukey RH, 40:581–618 Turko IV, 41:203–36

## U

Ulrich RG, 40:335-52

#### V

van der Sandt ICJ, 43:629-56 Venter JC, 40:97-132 Verma IM, 43:413-39

#### W

Walker CL, 39:295-312 Wallace KB, 40:353-88 Waring JF, 40:335-52 Waters N. 41:237-60 Watson RE, 42:501-25 Wehrens XHT, 43:441-61 Wei L-N, 43:47-72 Weiner JA, 41:507-34 Weinshilboum RM, 39:19-52 Wenthold RJ, 43:335-58 White RE, 40:133-57 Whitlock JP Jr, 39:103-25 Wong CF, 43:31-45 Wong YH, 40:389-430 Wood AJJ, 41:815-50 Wright GD, 42:381-408

## X

Xie H-G, 41:815-50

#### Y

Yaksh TL, 42:553–83 Yamakura T, 41:23–51 Yamazoe Y, 40:159–76 Yanagisawa M, 41:851–76 Yang CS, 42:25–54 Yoshimura N, 41:691–721

#### 7

Zhang Z-Y, 42:209-34 Zheng B, 40:235-71

## **CHAPTER TITLES, VOLUMES 39-43**

Induction of Drug-Metabolizing Enzymes:
A Path to the Discovery of Multiple

## **Prefatory**

### PHARMACOLOGY

Targets of Drug Action A Burgen 40:1–16
High-Throughput Screening in Drug
Metabolism and Pharmacokinetic
Support of Drug Discovery RE White 40:133–57

## TOXICOLOGY

Laboratory of Chemical Pharmacology, National Heart, Lung, and Blood JR Gillette 40:19-41 Institute, NIH: A Short History Chlorinated Methanes and Liver Injury: Highlights of the Past 50 Years GL Plaa 40:43-65 Central Role of Peroxisome Proliferator-Activated Receptors in the Actions of Peroxisome Proliferators JC Corton. 40:491-518 SP Anderson. A Stauber J Doull 41:1-21 Toxicology Comes of Age

## Cytochromes P450 AH Conney General Topics in Pharmacology and Toxicology

Hormesis: The Dose-Response Revolution

Regulatory Mechanisms Controllong Gene
Expression Mediated by the Antioxidant
Response Element

T Nguyen,
PJ Sherratt.

**CB** Pickett

43:1-30

#### RECEPTORS

- Genetic Regulation of Glutamate Receptor

  Ion Channels

  SJ Myers, 39:221-41

  R Dingledine,

  K Borges
- New Insights into Dopaminergic Receptor
  Function Using Antisense and
  Genetically Altered Animals

  DR Sibley

  39:313-41

Drug Discovery  TA Branchek, TP Blackbum  Nicotinic Receptors at the Amino Acid Level P-J Corringer, N Le Novère, J-P Changeux  RA North, A Surprenant Lysophospholipid Receptors N Fukushima, I Ishii, JJ Contos, JA Weiner, J Chun  Genetic Variations and Polymorphisms of G Protein-Coupled Receptors: Functional and Therapeutic Implications Prostanoid Receptors: Subtypes and Signaling RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection J Linden 41:773 Glutamatergic Mechanisms in	-58 -80 '-34
Level  P-J Corringer, N Le Novère, J-P Changeux  RA North, A Surprenant  Lysophospholipid Receptors  Lysophospholipid Receptors  P-J Corringer, N Le Novère, J-P Changeux  RA North, A Surprenant  N Fukushima, I Ishii, JJ Contos, JA Weiner, J Chun  Genetic Variations and Polymorphisms of G Protein-Coupled Receptors: Functional and Therapeutic Implications  PA Insel  Prostanoid Receptors: Subtypes and Signaling  RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury  DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection J Linden  41:775  Glutamatergic Mechanisms in	1–80 7–34
Pharmacology of Clonded P2X Receptors  Pharmacology of Clonded P2X Receptors  RA North, A Surprenant  N Fukushima, I Ishii, JJ Contos, JA Weiner, J Chun  Genetic Variations and Polymorphisms of G Protein-Coupled Receptors: Functional and Therapeutic Implications  Prostanoid Receptors: Subtypes and Signaling  RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury  Por Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	1–80 7–34
Pharmacology of Clonded P2X Receptors  RA North, A Surprenant  N Fukushima, I Ishii, JJ Contos, JA Weiner, J Chun  Genetic Variations and Polymorphisms of G Protein-Coupled Receptors: Functional and Therapeutic Implications Prostanoid Receptors: Subtypes and Signaling  RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	7–34
Genetic Variations and Polymorphisms of G Protein-Coupled Receptors: Functional and Therapeutic Implications  Prostanoid Receptors: Subtypes and Signaling  RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury  DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	
G Protein-Coupled Receptors: Functional and Therapeutic Implications PA Insel  Prostanoid Receptors: Subtypes and Signaling RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	-624
PA Insel  Prostanoid Receptors: Subtypes and Signaling RM Breyer, 41:661  CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection J Linden 41:775  Glutamatergic Mechanisms in	<b>⊢624</b>
Signaling  RM Breyer, CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in  41:773	
CK Bagdassarian, SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection J Linden 41:775  Glutamatergic Mechanisms in	
SA Myers, MD Breyer  Role of Osteopontin in Cellular Signaling and Toxicant Injury DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	-90
Role of Osteopontin in Cellular Signaling and Toxicant Injury  DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	
Role of Osteopontin in Cellular Signaling and Toxicant Injury  DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in  DT Denhardt, SR Rittling  DT Denhardt, SR Rittling  41:773	
and Toxicant Injury  DT Denhardt, CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in  41:773	
CM Giachelli, SR Rittling  Molecular Approach to Adenosine Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in	10
Receptors: Receptor-Mediated Mechanisms of Tissue Protection Glutamatergic Mechanisms in  J Linden 41:775	-49
Glutamatergic Mechanisms in	
	-87
Schizophrenia G Tsai, JT Coyle 42:165	-79
Drug Efficacy at G Protein-Coupled Receptors T Kenakin 42:349	70
Dimerization: An Emerging Concept for	-19
G Protein-Coupled Receptor Ontogeny	
and Function S Angers, 42:409	1_35
A Salahpour,	55
M Bouvier	
The Binding Site of Aminergic	
G Protein-Coupled Receptors: The	
Transmembrane Segments and Second	
Extracellular Loop L Shi, JA Javitch 42:43	1-67
Retinoid Receptors and Their Coregulators L-N Wei 43:47-	
Trafficking of NMDA Receptors  RJ Wenthold, 43:33:  K Prybylowski,  S Standley, N Sans,	i–58
RS Petralia	

RENAL SYSTEM		
Pharmacology of the Lower Urinary Tract	WC de Groat, N Yoshimura	41:691–721
SIGNAL TRANSDUCTION		
Physiological Functions of Cyclic ADP-Ribose and NAADP as Calcium	1101	41.217.45
Messengers Cellular Mechanisms for the Repression of	HC Lee	41:317–45
Apoptosis	CD Bortner, JA Cidlowski	42:259–81
SYNAPTIC FUNCTIONS		
Inhibition of Nitric Oxide Synthase as a		
Potential Therapeutic Target	AJ Hobbs, A Higgs, S Moncada	39:191–220
Redox Regulation of c-Ha-ras and Osteopontin Signaling in Vascular Smooth Muscle Cells: Implications in		
Chemical Atherogenesis	KS Ramos	39:243-65
Cyclins and Cell Cycle Checkpoints	DG Johnson, CL Walker	39:295–312
The Regulator of G Protein Signaling		
Family	L De Vries, B Zheng, T Fischer, E Elenko, MG Farquhar	40:235–71
Pharmacology of Selectin Inhibitors in		
Ischemia/Reperfusion States The Role of Rho in G Protein Coupled	DJ Lefer	40:283–94
Receptor Signal Transduction	VP Sah, TM Seasholtz, SA Sagi, JH Brown	40:459–89
14-3-3-Proteins: Structure, Function, and		
Regulations	H Fu, RR Subramanian, SC Masters	40:619–49
Molecular Psychology: Roles for the ERK MAP Kinase Cascade in Memory	JP Adams, JD Sweatt	42:135–63
TRANSPORTERS		
Compartmentation of G Protein-Coupled		
Signaling Pathways in Cardiac Myocytes	SF Steinberg, LL Brunton LL	41:751–73
<b>AKAP-Mediated Signal Transduction</b>	JJC Michel, JD Scott	42:235-57

The Changing Face of the Na <sup>+</sup> /H <sup>+</sup>		
Exchanger, NHE1: Structure,		
Regulation, and Cellular Actions	LK Putney,	42:527-52
	SP Denker,	
	DL Barber	
Monoamine Transporters: From Genes to		
Behavior	RR Gainetdinov,	43:261-84
	MG Caron	
Genetic Polymorphisms of the Human		
MDR1 Drug Transporter	M Schwab,	43:285–307
	M Eichelbaum,	
	MF Fromm	
The Caenorhabditis elegans Dopaminergic		
System: Opportunities for Insights into		
Dopamine Transport and		
Neurodegeneration	R Nass, RD Blakely	43:521-44
The Role of Drug Transporters at the		
Blood-Brain Barrier	AG de Boer,	43:629-56
	ICJ van der Sandt,	
	PJ Gaillard	
ENZYMES		
Methylation Pharmacogenetics: Catechol		
O-Methyltransferase, Thiopurine		
Methyltransferase, and Histamine		
N-Methyltransferase	RM Weinshilboum,	39:19-52
11 112001 / 101001010101010	DM Otterness.	
	CL Szumlanski	
Regulation and Inhibition of Phospholipase A <sub>2</sub>	J Balsinde.	39:175-89
rioguitton and minoriton of 1 moophone 1-2	MA Balboa,	
	PA Insel.	
	EA Dennis	
Human UDP-Glucuronosyltransferases:		
Metabolism, Expression, and Disease	RH Tukey,	40:581-618
Methodishi, Expression, and Disease	CP Strassburg	101000 011
Tumor Cell Death Induced by	or badoodag	
Topoisomerase-Targeting Drugs	T-K Li, LF Liu	41:53-77
Phenobarbital Response Elements of	1 11 21, 21 210	12.00
Cytochrome P450 Genes and Nuclear		
Receptors	T Sueyoshi,	41:123-43
Receptors	M Negishi	41.125 45
Regulation and Role of Adenylyl Cyclase	MI MCRISIN	
	J Hanoune, N Defer	41:145-74
Isoforms Regulation of CYP3A Gene Transcription	5 Handane, 14 Deter	41.145-74
	B Goodwin,	42:1-23
by the Pregnane X Receptor	MR Redinbo.	74.1-43
	SA Kliewer	
	SA KIICWEI	

Protein Allergenicity Assessment of Foods		
Produced Through Agricultural		
Biotechnology	SL Taylor	42:99-112
The Biochemistry and Physiology of S-Nitrosothiols	N Hogg	42:585600
Telomere Inhibition and Telomere	Nilogg	42.363-000
Disruption as Processes for Drug		
Targeting	EM Rezler,	43:359-79
	DJ Bearss,	
	LH Hurley	
CHEMICAL AGENTS		
The Pineal Gland and Melatonin:		
Molecular and Pharmacologic		
Regulation	J Borjigin, X Li, SH Snyder	39:53–65
Regulation of Gene Expression		
by Reactive Oxygen	TP Dalton, HG Shertzer,	39:67–101
Cutatoriaity of Short Chain Alashala	A Puga RC Baker, RE Kramer	39:127-50
Cytotoxicity of Short-Chain Alcohols Metallothionein: An Intracellular Protein	RC Baker, RE Krainer	39.127-30
to Protect Against Cadmium Toxicity	CD Klaassen, J Liu,	39:267-94
to 1100001 against Cummum 10mony	S Choudhuri	071201 71
Teratology of Retinoids	MD Collins, GE Mao	39:399-430
The Clinical Pharmacology of L-Arginine	RH Böger,	41:79-99
	SM Bode-Böger	
The Basic and Clinical Pharmacology of		
Nonpeptide Vasopressin Receptor		
Antagonists	M Thibonnier,	41:175–202
	P Coles,	
	A Thibonnier, M Shoham	
Novel Effects of Nitric Oxide	KL Davis, E Martin,	41:203-36
Novel Effects of Patric Oxide	IV Turko, F Murad	41.205-50
Inhibition of Carcinogenesis by Tea	CS Yang, P Maliakal,	42:25-54
	X Meng	
Nitric Oxide-Releasing Drugs	C Napoli, LJ Ignarro	43:97-123
2,5-Hexandione-Induced Testicular Injury	K Boekelheide,	43:125-47
	SL Fleming,	
	T Allio,	
	ME Embree-Ku,	
	SJ Hall,	
	KJ Johnson,	
	EJ Kwon, SR Patel,	
	RJ Rasoulpour, HA Schoenfeld,	
	S Thompson	
	3 i nompson	

Progress Toward Clinical Application of		
the Nitric Oxide-Releasing Diazeniumdiolates	LK Keefer	43:585–607
PEPTIDES AND PROTEINS		
Protein Allergenicity Assessment of Foods Produced Through Agricultural Biotechnology	CI Taulan	42.00 112
Biotechnology	SL Taylor	42:99–112
BIOTRANSFORMATION		
Cytochrome P-450 3A4: Regulation and		
Role in Drug Metabolism	FP Guengerich	39:1-17
Induction of Cytochrome P4501A1	JP Whitlock Jr	39:103-25
Metabolism of Fluorine-Containing Drugs	BK Park, NR Kitteringham, PM O'Neill	41:443–70
Interindividual Variability in Inhibition and		
Induction of Cytochrome P450 Enzymes	JH Lin, AYH Lu	41:535–67
Regulation of CYP3A Gene Transcription		
by the Pregnane X Receptor	B Goodwin, MR Redinbo, SA Kliewer	42:1–23
Human Extrahepatic Cytochromes P450: Function in Xenobiotic Metabolism and Tissue-Selective Chemical Toxicity in the Respiratory and Gastrointestinal		
Tracts	X Ding, LS Kaminsky	43:149-73
NUCLEIC ACIDS		
Cellular Responses to DNA Damage	CJ Norbury, ID Hickson	41:367–401
Ca <sup>2+</sup> /CaM-Dependent Kinases: From		
Activation to Function	SS Hook, AR Means	41:471–505
PHARMACOKINETICS/TOXICOKINETICS		
Biochemical, Cellular, and Pharmacological Aspects of the		
Multidrug Transporter	SV Ambudkar, S Dey, CA Hrycyna, M Ramachandra, I Pastan, MM Gottesman	39:361–97
Mitochondrial Targets of Drug Toxicity	KB Wallace, AA Starkov	40:353–88

CANCER AND CARCINOGENESIS		
Properties and Biological Activities of		
Thioredoxins	G Powis, WR Montfort	41:261–95
Cancer Chemoprevention Using Natural		
Vitamin D and Synthetic Analogs	KZ Guyton, TW Kensler, GH Posner	41:421–42
Inhibition of Carcinogenesis by Tea	CS Yang, P Maliakal, X Meng	42:25–54
COX-2: A Target for Colon Cancer		
Prevention	LJ Marnett, RN DuBois	42:55–80
Glycopeptide Antibiotic Resistance	J Pootoolal, J Neu, GD Wright	42:381–408
Altered DNA Methylation: A Secondary		
Mechanism Involved in Carcinogenesis	JI Goodman, RE Watson	42:501–25
Signal Transduction-Directed Cancer		
Treatments	EA Sausville, Y Elsayed, M Monga, G Kim	43:199–231
CLINICAL THERAPEUTICS		
Dual Protease Inhibitor Therapy in		
HIV-Infected Patients: Pharmacologic		
Rationale and Clinical Benefits	C Flexner	40:651-76
Pharmacogenomics: Unlocking the Human		
Genome for Better Drug Therapy	HL McLeod, WE Evans	41:101-21
Antisense Oligonucleotides:		
Promise and Reality Glycopeptide Antibiotic Resistance	I Lebedeva, CA Stein J Pootoolal, J Neu, GD Wright	41:403–19 42:381–408
Complementary and Alternative	OD Wilgin	
Therapeutics: Rigorous Research is		
Needed to Support Claims	JF Kinsel, SE Straus	43:463-84
DRUG DEVELOPMENT SCIENCE		
Parallel Array and Mixture-Based Synthetic Combinatorial Chemistry:	DA Warahara	40:273–82
Tools for the Next Millennium A Novel Means of Drug Delivery: Myoblast-Mediated Gene Therapy and	RA Houghten	40:213-82
Regulatable Retroviral Vectors	CR Ozawa, ML Springer,	40:295–317

**HM Blau** 

Use of Biomarkers and Surrogate Endpoints in Drug Development and Regulatory Decision Making: Criteria,		
Validation, Strategies	L Lesko, AJ Atkinson Jr.	41:347–66
Molecular Basis of Environmentally	AJ AIKIISOII JI.	
Induced Birth Defects	RH Finnell, J Gelineau-van Waes, JD Eudy, TH Rosenquist	42:181–208
Protein Tyrosine Phosphatases: Structure and Function, Substrate Specificity, and		
Inhibitor Development Designing Inhibitors of Cyclin-Dependent	Z-Y Zhang	42:209–34
Kinases	IR Hardcastle, BT Golding, RJ Griffin	42:325–48
Protein Flexibility and Computer-Aided		
Drug Design	CF Wong,  JA McCammon	43:31–45
Gene Therapy with Viral Vectors	NA Kootstra, IM Verma	43:413–39
Systems		
IMMUNE SYSTEM/INFLAMMATION		
Signal Transduction by Cell Adhesion Receptors and the Cytoskeleton: Functions of Integrins, Cadherins, Selectins, and Immunoglobulin-		
Superfamily Members Structure, Function, and Inhibition of	RL Juliano	42:283–323
Chemokines Innate Immune Responses to Microbial	EJ Fernandez, E Lolis	42:469–99
Poisons: Discovery and Function of the Toll-Like Receptors	B Beutler	43:609–28
CENTRAL NERVOUS SYSTEM		
Glial Cells in Neurotoxicity Development	M Aschner, JW Allen, HK Kimelberg, RM LoPachin, WJ Streit	39:151–73
Excitatory Amino Acid Transporters:		
A Family in Flux	RP Seal, SG Amara	39:431–56

Molecular Mechanisms and Regulation of		
Opiod Receptor Signaling	P-Y Law, YH Wong, HH Loh	40:389–430
Anesthetics and Ion Channels: Molecular		
Models and Sites of Action	T Yamakura, E Bertaccini, JR Trudell, RA Harris	41:23–51
Interactions Between Monoamines,		
Glutamate, and GABA in		
Schizophrenia: New Evidence	A Carlsson, N Waters, S Holm-Waters, J Tedroff, M Nilsson, ML Carlsson	41:237–60
Drug Treatment Effects on Disease		
Progression	P Chan, N Holford	41:625-59
Molecular Targets of Lithium Action	CJ Phiel, PS Klein	41:789-813
Neurokinin1 Receptor Antagonists as		
Potential Antidepressants	SC Stout, MJ Owens, CB Nemeroff	41:877–906
Glutamatergic Mechanisms in		
Schizophrenia	G Tsai, JT Coyle	42:165–79
The Spinal Phospholipase-		
Cyclooxygenase-Prostanoid Cascade in		
Nociceptive Processing	CI Svensson, TL Yaksh	42:553–83
Alzheimer's Disease: Molecular		
Understanding Predicts Amyloid-Based		
Therapeutics	DJ Selkoe, D Schenk	43:545–84
AUTONOMIC NERVOUS SYSTEM		
$\beta$ -Adrenergic Receptors and Receptor		
Signaling in Heart Failure	SR Post, HK Hammond, PA Insel	39:343–60
Genetic Variations and Polymorphisms of		
G Protein-Coupled Receptors:		
Functional and Therapeutic Implications	BK Rana, T Shiina, PA Insel	41:593–624
CARDIOVASCULAR SYSTEM		
Endothelin System: The Double-Edged		
Sword in Health and Disease	RM Kedzierski,	41:851-76
	M Yanagisawa	

K+ Channel Structure-Activity		
Relationships and Mechanisms of Drug-Induced QT Prolongation	CE Clancy, J Kurokawa, M Tateyama, XHT Wehrens, RS Kass	43:441–61
ENDOCRINE SYSTEM		
Neurotrophic and Neuroprotective Actions of Estrogens and Their Therapeutic Implications	SJ Lee, BS McEwen	41:569–91
PULMONARY SYSTEM		
Cytokine Modulators as Novel Therapies for Asthma Novel Pharmacological Approaches to	PJ Barnes	42:81–98
Manage Interstitial Lung Fibrosis in the Twenty-First Century	SN Giri	43:73–95
Miscellaneous		
TECHNIQUES		
The Impact of Genomics-Based Technologies on Drug Safety Evaluation Challenges for Biomedical Informatics and Pharmacogenomics	JF Waring, RG Ulrich RB Altman, TE Klein	40:335–52 42:113–33
ENVIRONMENTAL TOXICITY		
The PAS Superfamily: Sensors of Environmental and Developmental		
Signals	Y-Z Gu,  JB Hogenesch,  CA Bradfield	40:519–61
Challenging Dogma: Thresholds for Genotoxic Carcinogens? The Case of		
Vinyl Acetate	JG Hengstler, MS Bogdanffy, HM Bolt, F Oesch	43:485–520
Pharmacology and Toxicology in the	New Millennium	
Pharmacokinetic/Pharmacodynamic		
Modeling in Drug Development	LB Sheiner,	40:67–96

J-L Steimer

Sequencing the Entire Genomes of Free-Living Organisms: The Foundation of Pharmacology in the New Millenium S Broder, JC Venter 40:97-132 High-Throughput Screening in Drug Metabolism and Pharmacokinetic **RE White** Support of Drug Discovery 40:133-57 Pharmacogenetics of Sulfotransferase 40:159-76 K Nagata, Y Yamazoe EH Ohlstein, Drug Discovery in the Next Millennium 40:177-91 RR Ruffolo Jr, JD Elliott The Impact of Genomics on Drug C Debouck, B Metcalf Discovery 40:193-208 NHG Holford. 40:209-34 Simulation of Clinical Trials HC Kimko, JPR Monteleone,

CC Peck

